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Editorial

Stem Cell Therapy: Future of Pain Medicine

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Nearly 30% of seniors have chronic musculoskeletal pain. The most common cause of pain in seniors is related to the degenerative changes of the spine and joints[9]. Conventional treatments are often restricted to the management of symptoms. Use of chronic anti-inflammatory medications in seniors may bear serious risks in gastrointestinal and renal systems. Physical therapy has limited value. Epidural steroid injection(s) may provide up to three months of pain relief. However, there are some risks involved. Spine surgery for degenerative spine diseases has a limited success rate. Up to 30% or 40% of patients may continue to have pain after back surgery. Surgical repair of a knee injury and knee replacement surgeries are popular. However, the costs are relatively high. Many senior patients may not be ideal candidates for surgery due to cardiovascular conditions. Furthermore, all these treatments do not address the key cause of spine and joint pain due to degeneration of cells and subsequent tissue damage[9]. Recent development in stem cells therapy (SCT) has provided a new hope for seniors.

Back Pain

The major cause of back pain is the degeneration of the cells in the intervertebral discs. Over the last few years molecular, cell-based therapies and tissue-engineering strategies with SCT for disc regeneration have significantly increased. A recent report showed that injection of mesenchymal stem cells (MSC) into bovine intervertebral discs can increase the expression of extracellular type II collagen and maximize extracellular matrix production[7]. Chun et al [1]injected human adipose-derived stem cells (ADSCs) into 20 mature male New Zealand white rabbits. The proliferation of ADSCs at the L4-5 disc was found at 10 weeks after cell injection. Histologically, the ADSC-injected discs exhibited elevated extracellular matrix secretion and little ossification of damaged cartilage in the nucleus pulposus compared with degenerative control discs.

In addition to the promising results from animal research, preliminary human studies showed mixed results. In 2006, Haufe et al[3] reported 10 patients who underwent intradiscal injection of hematopoietic precursor stem cells (HSCs) obtained from their pelvic bone marrow. Of the 10 patients, none achieved any improvement of their discogenic low back pain after one year follow-up. More recently Orozco et al [8] reported a study of ten patients with chronic back pain treated with intradiscal injection of autologous expanded bone marrow MSC. Patients were followed for 1 year. Rapid improvements of pain and disability were reported (85% of maximum in 3 months). Although disc height was not recovered, water content was significantly elevated at 12 months. Advantages of intradiscal MSC therapy include simpler and preservation of normal biomechanics without surgery. However, long term survival of the transplanted MSCs in the harsh environment of the discs is still a major challenge. To the date, no double-blind, controlled studies have been published to confirm the clinical efficacy of SCT for the pain due to degenerative disc diseases.

Knee Pain

It is estimated there will be seven-fold increase in knee replacements in the United States between 2005 and 2030. However, SCT may reduce the future need for knee replacement[5]. Autologous MSC and ex vivo expanded skeletal SC all have shown promising results in the treatment of knee pain caused by osteoarthritis (OA).

In an experimental animal meniscus injury model, it has been reported [10] that transplantation of human meniscus stem/progenitor cells (hMeSPCs) effectively protected articular cartilage, promoted neo-tissue formation with better-defined shape and more matured extracellular matrix and smother surface cartilage, and maintained joint space at 12 weeks postsurgery[11]. MSC therapy may also reduce animal pain behavior[14].

In human studies, Turajane et al[13] conducted a case-series study with five patients that failed conservative treatment. It was reported that the combination of intra-articular autologous activated peripheral blood stem cells with growth factor addition/preservation along with hyaluronic acid in conjunction with arthroscopic microdrilling MCS resulted in Quality of Life improvements and succeeded in regenerating articular cartilage in early osteoarthritic knee disease. Skowronski[12]reported 52 patients treated with autologous blood MSC for knee pain due to cartilage lesions. Scores improved across all scales with an average improvement of 23 points in the Knee Injury and

Osteoarthritis Outcome Score scale and 35 points in the Lysholm knee scale at one year.

Koh et al[4] treated eighteen patients with injection of autologous fat pad-derived MSC for knee pain due to OA. Patients were followed for 24 to 26 months after therapy. Western Ontario and McMaster Universities Osteoarthritis Index, Lyholm scores as well as VAS scores all significantly improved. Radiographic study showed the whole-organ MRI score had significantly improved from 60.0 points to 48.3 points at the final follow-up point. Particularly notable was the change in cartilage whole-organ MRI score, which improved from 28.3 points to 21.7 points. More recently, Vangsness et al reported[15]a randomized, double-blind, controlled study on adult human MSC delivered via intra-articular injection to the knee following partial medial meniscectomy. A single superolateral knee injection was given to 55 patients within seven to ten days after the meniscectomy. It was found that there was significantly increased meniscal volume determined by quantitative MRI in groups that received SCT. No patients in the control group had significant increase in meniscal volume. Patients with osteoarthritic changes who received MSC experienced a significant reduction in pain compared with those who received the control. This randomized, double-blind, controlled study confirmed that MSC could be a promising treatment for knee pain due to osteoarthritis and meniscus tear.

Challenges for SCT

The advantage of SCT is that stem cells can regenerate healthy and functionally specialized cells and tissues to replace the destroyed or degenerative tissues. Though it is promising, it is still facing a variety of challenges. Firstly, there are many studies reporting the clinical efficacy, most studies are open label. Only few, if any, double-blind, controlled studies have supported the efficacy of SCT for knee pain due to osteoarthritis. To the date, there are no controlled studies confirming the clinical efficacy of SCT for degenerative spine diseases. Thus more clinical studies are needed. Secondly, biological techniques for stem cell transplantation are waiting to be enhanced. For example, the stem cells transplanted into degenerated intervertebral discs will face a harsh environment, which has very high pressure, low nutrition and low oxygen. To enhance the cell survival rate and ensure the transplanted cells differentiating toward chondrocyte-like cells, which can produce proteoglycans and type II collagen, more basic science studies are needed[2]. The third challenge for SCT is iatrogenic cancerogenesis. Embryonic stem cells, including totipotent stem cells (produced from fusion of egg and sperm), and pluripotent stem cells (5-14 day old blastocytes) have a strong potency of cell reproducing and potentially highly teratogenic. Novel strategies such as using transgenic expression of the genetically engineered human recombinant DNases in proliferating and directed differentiation resisting stem cells are being developed to inhibit or prevent the iatrogenic cancerogenesis[6]. Adult SCs (Adipose, peripheral and bone marrow derived SCs) have the ability to differentiate and form a variety of tissues. These adult SCs have been used in researches to treat variety of human diseases. So far no iatrogenic carcinomas have been reported as the results of the treatment. The fourth major issue related to SCT is the legal challenge. Worldwide, different countries have different laws on SC research and use. Even President Barack Obama signed an executive order on March 9, 2009 to lift the restrictions on federally funded human embryonic stem cells (hESC) research, currently only adult stem cells (adipose, peripheral and bone marrow derived stem cells) are allowed to be used in most clinical settings. These cells should be minimally manipulated. Use of hESC from fetus, umbilical cord and amniotic fluid are all limited for research purposes. Researchers and clinicians must be familiar with the laws of their respective countries and states before becoming involved in SC therapy or research.

Conclusion

The treatment of chronic pain conditions is constantly evolving. Recent advancements in SCT for pain due to degenerative diseases in the spine and joints are promising and indicative that SCT will undoubtedly play a major role in the future. However, more studies are needed to enhance the biological techniques, confirm the clinical efficacy, reduce the risk of iatrogenic carcinoma and address the legal issues related to this exciting treatment. It is likely that SCT will be utilized more extensively in the future for replacing diseased tissues as an alternative to open back surgery or joint replacement.

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None
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