Case Report

Mesenchymal Stem Cell Injection in Two Patients Suffer From Chronic Discogenic Low Back Pain

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Abstract

Background: Discogenic low back pain is one of the leading causes of pain and disability across the world. A growing interest in the area of regenerative medicine, led by an improved understanding of the role of mesenchymal stem cells in tissue homeostasis and repair.

Cases Report: We had two patients suffered from chronic discogenic low back pain. They were underwent injection of intra-discal 1.5 cc of Adipose Derived Mesenchymal Stem Cells (ADMSC) and followed up for 6 months. After this period of time, there was a significant reduction in both VAS and ODI scores in patients.

Conclusion: These data warrant further studies so that we can enhance our understanding of the other unknown mechanisms, which may exist behind stem cell injection. If the effectiveness of such injection to reduce pain and improve function is shown in the upcoming studies, it may provide a new insight for increasing this method of treatment as a proper option in the near future.

Keywords: Low back pain, Pain management, Stem cell

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Introduction

Low back pain (LBP) is one of the leading causes of disability and has enormous social and economic impact of patients and their family members[1,2]. Approximately 80% of adults experience LBP at some point in their lifetime, with a prevalence ranging from 15 to 45%, and the prevalence of chronic LBP increases with age due to global population aging, changes in lifestyle, and occupational stresses[2-4].

Intervertebral disc (IVD) degeneration is characterized by progressive and irreversible IVD degradation due to many different causes[2-4]. The causes of this degeneration are complex and multifactorial, and include genetic, nutritional, and mechanical influences[2,5]. Intervertebral disc degeneration is characterized by progressive decline in nucleus pulposus (NP) hydration due to the loss of extracellular matrix (ECM) molecules such as aggrecan and collagen[2,5]. This dehydration of disc could lead to a loss of mechanical tension in the collagen fibers of the annulus fibrosis and result in abnormal spinal axial

loading forces and segmental instability[6]. Eventually, IVD degeneration can result in abnormalities of other parts of the IVD such as endplate and facet joint and develop into serious conditions, or facet joint syndrome[7,8].

The surgical procedures to correct herniated disc or spinal stenosis caused by IVD degeneration do not address the abnormal increase in pro-inflammatory cytokine levels of the degenerated disc or the inherent loss of functional native cells within the IVD. Our research is focusing on the development of stem cell-based therapies to inhibit aberrant cytokine production, stimulate matrix anabolism production, and repopulate and influence the native cells. IRB approval was obtained from Shahid Beheshti University of Medical Sciences (IR.SBMU.REC.1397.045).

Several adult stem cell types have been applied in preclinical and clinical studies[2, 9-11], and mesenchymal stem cells (MSCs) have been anticipated as an ideal cell source for IVD regeneration because of their immune-modulatory functions and capacity for cartilage differentiation. Few studies as a human clinical trial demonstrated improved pain and disability scores as well as increased water content in the disc 12 month after MSC implantation[9-11]. MSCs implantation in degenerated IVD may induce osteophyte formation by cell leakage.

Case Report

Case 1: A 40 year old female complained of lumbar back pain for 10 years, she had not any history of disease except for hypothyroidism, which was under control, and the lab tests were within normal limit. According to the MRI, the disc of L5-S1 was involved. Preoperative VAS score and ODI score were 8 and 32, respectively. The preoperative Pfirrmann score was assessed grade IV for this patient. After injection of 12×10^{6} ADMSC in 1.5 ml, the ODI score was measured at 1 week (wk), 1, 3 and 6 months after injection. This score was 32 at 1 wk, 28 at 1, 3 and 6 months after injection. The VAS score at 1 wk was the same as pre-operation score. At 1 month and 3 months after injection, 70% reduction in VAS pain score was seen. At 6 months after injection, this reduction reached 80% improvement compare to pre-operation.

Case 2: A 37 year old male complained of lumbar back pain with no history of any disease and the lab tests were within normal limit. Preoperative VAS, and ODI scores was 7, and 28, respectively. The preoperative Pfirrmann score was also assessed grade IV for this patient. After injection of 10^{7} cells ADMSC in 1.5 ml, the ODI score was measured at 1 wk, 1, 3 and 6 months after injection. This score was 30 at 1 wk, 20 at 1, 3 and 6 months after injection. The VAS score at 1 wk was the same as pre-operation score, At 1 month and 3 months after injection 40% reduction in VAS score was seen. At 6 months after injection, this reduction reached 70% improvement compared to pre-operation.

Discussion

MSC-based intradiscal treatment has recently attracted attention for its potential to revolutionize the treatment of chronic discogenic LBP by repopulating the IVD and restoring functional tissue through matrix synthesis by implanted cells and possible beneficial effects on native cells[4]. At least four published studies have used MSC-based therapies to treat chronic discogenic LBP[9,10,12]. Yoshikawa et al[10] first reported significant LBP reduction and rehydration of the treated disc following percutaneous injection of autologous BM-MSCs within a collagen sponge in two older patients with markedly degenerated disc. Orozco et al[9] reported pilot study of 10 patient with chronic discogenic LBP treated with percutaneous intradiscal injection of autologous BM-MSCs, in which 90% of patient reported clinical benefit, and both LBP and disability were greatly reduced at 3 months after transplantation, followed by modest additional improvement at 6 and 12 months. MRI also showed marginally improved hydration of the treated disc at 12 months[6-9]. Pettine et al[12] evaluated the use of autologous, concentrated BM cells considered to contain multiple stem and progenitor cells, including MSCs, and demonstrated significant improvement in the VAS, ODI, and modifier Pfirrmann score at 3, 6 and 12 months post transplantation. In their study, patients who received more than 200 colony-forming unit-fibroblasts (CFU-F) per milliliter of bone marrow aspirate showed significantly greater improvement of discogenic LBP compared to the others.

In another study conducted by Kumar et al[13] it was revealed that combined adipose tissue-derived mesenchymal stem cells (AT-MSC) and hyaluronic acid derivative in chronic discogenic LBP is safe and

tolerable and among six patients who achieved significant improvement in VAS, and ODI three patients determined to have increased apparent diffusion coefficient on diffusion MRI.

However, we assume that injection of MSCs into the degenerated disc improves ECM production by degenerated host NP cells, increases NP-like gene expression, and modulates the immunological response of NP cells to inflammatory cytokines. The immune-modulatory effects of MSCs on NP cells within the degenerated disc could potentially inhibit the inflammatory cascade, thereby preventing ingrowth of pain-inducing vasculature and nerve fibers[2,8,12-17].

Conclusion

These data warrant further studies so that we can enhance our understanding of the other unknown mechanisms, which may exist behind stem cell injection. If the effectiveness of such injection to reduce pain and improve function is shown in the upcoming studies, it may provide a new insight for increasing this method of treatment as a proper option in the near future.

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