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Mesenchymal stem cell and osteoarthritis: a literature review

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ABSTRACT

The most common disease in the aged population is osteoarthritis (OA) that is resulting in progressive dysfunction following isolated cartilage injuries, subchondral bone remodeling, tissue loss, marginal osteophytes, and loss of joint space. Mesenchymal stem cells (MSCs) are multipotent stem cells; they are able to produce many or all joint tissues. Bone marrow and adipose tissue are rich sources of mesenchymal cells that are useful for the reconstruction of injured tissues such as bone, cartilage, or cardiac muscle. Recently, some studies have been performed on the use of the direct intra-articular injection of mononuclear cells (MNCs) and MSCs as potential therapeutic targets in OA. In this review, the history of MSCs in the treatment of OA are explained. Injection of Bone Marrow Aspirates Concentrate (BMAC) has significantly improved both joint pain and function in radiologic findings; some studies suggested that the injection would be even more effective in early to moderate phases of OA. Injection of MSCs in combination with growth factors may be better solution for the treatment.

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Introduction

Osteoarthritis (OA) is a chronic degenerative process, resulting in progressive dysfunction following isolated cartilage injuries, subchondral bone remodeling, tissue loss, marginal osteophytes, and loss of joint space (1). Cartilage damage is a main problem in OA. The treatments, used for cartilage repair in OA, include medication therapy, surgical joint replacement, microfracture, and osteochondral graft transplantation (mosaicplasty) (2). Elderly patients undergo a total knee replacement. In younger patients with less damaged joints, attempts have been made to introduce cartilage regeneration for the prevention of joint dysfunction and replacment. Currently, with tissue engineering methods, stem cells may be able to be used for autologous chondrocyte implantation (ACI) strategies that provide an abundant cell source to repair OA (3). If the injection of mesenchymal stem cells (MSC) is effective for the treatment of OA, we could use this modality before other aggressive treatments such as joint surgery and replacement.

MSCs are multipotent stem cells that differentiate into various functional cell types of mesodermal tissues and have shown the ability to engraft and migrate into multiple musculoskeletal tissues (4,5). Bone marrow contains MSC progenitor cells of some

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mesenchymal tissues such as cartilage, bone, muscle, and fat (6). Tissue engineering combine MSCs with chondrogenic signals and various scaffolds to produce a functional tissue that could be used to repair focal cartilage defects (7).

Literature review

Recent recommendations have focused on intra-articular injection of MSCs as a therapy for OA. Autologous bone marrow-derived MSCs have been injected in different animal models of OA including Murphy et al. (8) injected MSCs into the knee joints of the goats, Toghraie et al. (9) used a rabbit model and Black et al. (10) used dog models. Results showed that the direct intra-articular injection of MSCs reduced the development of advanced OA lesions.

In vitro culture for osteogenic comparison, displayed properties of MSCs and detected sufficient bone matrix and bone-specific protein (osteoclacin) of bone marrow stem cells (BMSCs) under the osteogenic differentiation condition. In 2003, Ugarte et al. (11) reported no significant difference in osteogenic ability between human BMSCs and adipose tissue–derived MSCs (AMSCs). In 2005, Gun-II et al. (12) showed that human AMSCs have inferior osteogenic capabilities compared to BMSCs. In 2008, Hayeshi et al. (13) demonstrated that adult MSCs from bone marrow and periosteum could be considered ideal candidates for the regeneration of bone tissue. In 2006, Caplan et al. (14) and Agung et al. (15) revealed that intra-articular injection of MCSs into injured tissues could induce a host repair response to replace the injured tissue. The underlying mechanisms in the development of these novel therapeutic interventions modulate MSC to promote joint surface regeneration and influence the outcomes of joint disorders such as OA.

In clinical settings, MSCs could been also used for the regeneration and maintenance of articular cartilage in OA. In 2011, Pak reported stem cells injection into the right hip in two patients, obtained from adipose tissue; the following MRI images showed significant positive changes. They confirmed that stem cell therapy could improve OA and osteonecrosis of the femoral head (16).

Wolfstadt et al. investigated 214 adults with OA in USA from 1990 to 2013 in seven different clinical studies. MSCs had the potential for improving function and decreasing inflammation in patients with OA (17).

Between 2005 to 2009, Centeno et al. studied 227 patients who were treated for various orthopedic conditions with culture-expanded, bone marrow-derived MSCs. The pre- and postprocedure MRI analysis revealed increased meniscus and cartilage volume, and the modified visual analogue scale (VAS) scores decreased by 95% at three-month follow-up. Two subsequent studies from the same group using the same treatment procedure were conducted on a large group of patients suffering from OA and other intra-articular pathology; thus, MSC-related complications were generally infrequent, transient, or remediated with simple therapeutic measures (18,19).

In a study performed in Iran (2012) by Emadedin et al, intra-articular injection of culture-expanded MSCs was used for OA therapy in six females with radiological evidence of knee OA. Up to six months postinjection, all measured parameters improved (19).

Wong et al. investigated two groups of patients with OA in 2013 at Singapore. In first group, as a controlled clinical study, microfracturing (MFX) was combined with intra-articular injection of MSCs that was used for the treatment of unicompartmental OA knees undergoing high tibial osteotomy (HTO), whereas the second group of 28 patients received an intra-articular injection with hyaluronic acid. One year after surgical intervention, MRI scans showed significantly better Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) scores for the cell-recipient group. This result demonstrated that intra-articular injection of cultured MSCs was effective in the improvement of both short-term clinical and MOCART outcomes in patients undergoing HTO and MFX for varus knees with cartilage defects (20).

In a recent study in Germany, Kim et al. used combined intra-articular injection of autologous Bone Marrow Aspirates Concentrate (BMAC) with adipose tissue into the knees of 41 patients with OA. They showed significant improved pain and function of knee in all patients (21).

Davatchi et al. worked on four patients at Shariati Hospital, Tehran in 2011. The patients were aged 55, 57, 65, and 54 years, with moderate to severe knee OA and 30 mL of bone marrow was taken from each patient, and cultured for MSC growth. They showed pain improvement in three patients when walking and one patient remained unchanged (22).

In 2002, Wakitani et al. studied twenty-four knees of 24 patients with OA in Japan. They cultured adherent cells in bone marrow aspirates and embedded in collagen gel, transplanted into the articular cartilage defect in the medial femoral condyle. After 6.3 weeks, defects were covered and were covered with harder hyaline cartilage-like tissue 42 weeks after transplantation. They recommended transplantation of autologous culture expanded MSCs for the repair of articular cartilage defects in human (6).

In another study in 2013 at Poland, Skowroński et al. used Bone Marrow Concentrate (BMC) and collagen membrane in 54 patients with large cartilage

lesions of the knee. All scales of 52 patients were significantly improved without infectious complication. They reported that bone marrow stem cell injection was an effective modality for the reconstruction of large cartilage lesions (23).

Vangsness et al. performed treatment options for tissue restoration and the prevention of degenerative changes in the knee of 55 patients in 2014 at California, USA. Patients were randomized to one of the following treatment groups: in Group A, patients received 50 × 106 allogeneic MSCs; Group B, 150 × 106 MSCs; and the control group, a sodium hyaluronate. Twelve months after meniscectomy, there was a significant increase in meniscal volume in 24% patients of Group A and 6% patients of Group B. On the basis of VAS, MSC group experienced a significant reduction in pain compared with the control group (24).

Varma et al. selected 50 patients with mild to moderate knee OA in 2010 at India. They divided patients into two groups. Group A and B received arthroscopic debridement, but group B received mesenchymal stem cell concentrate injection as well. On the basis of VAS and OA outcome score, the technique used in this study considerably improved the overall OA outcome score, especially the quality of life (25).

Conclusion

Findings from the studies showed that BMC had important clinical implications which could be applied in OA treatment. The aforementioned methods have shown that the injection of MSCs alone or in combination with growth factors might be a better solution for the treatment of OA. MSCs injection was effective for the treatment of OA; thus, we could use this modality in clinical trials.

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Conflict of Interest

The authors declare no conflict of interest.

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