CLINICAL STUDY

Intra-articular Injection of Mesenchymal Stem Cells and Platelet-Rich Plasma to Treat Patellofemoral Osteoarthritis: Preliminary Results of a Long-Term Pilot Study

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ABSTRACT

Purpose: To assess the feasibility and safety of concomitant intra-articular (IA) knee injection of mesenchymal stem cells (MSCs) and platelet-rich plasma (PRP) under fluoroscopic guidance to treat patellofemoral osteoarthritis (OA).

Materials and Methods: This prospective study included 19 consecutive patients referred for fluoroscopically guided IA MSC and PRP injection for symptomatic patellofemoral chondropathy in which conservative treatment had failed. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and magnetic resonance (MR) data, including T2 mapping sequence, were prospectively collected before and 6 months after treatment. Clinical data without MR imaging were collected until 12 months after the procedure.

Results: WOMAC scores were significantly lower after IA injection of MSCs and PRP at 6 months and during 12-months follow-up compared with baseline (mean score decreased from 34.3 to 14.2; $P < .0018$). Patients reported no complications. Concerning MR imaging follow-up, there were no significant differences in grade, surface, or T2 value of the chondral lesions ($P > .375$).

Conclusions: IA injection of MSCs and PRP in early patellofemoral OA appears to allow functional improvement.

ABBREVIATIONS

IA = intra-articular, MSC = mesenchymal stem cell, OA = osteoarthritis, PRP = platelet-rich plasma, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Osteoarthritis (OA) is a chronic degenerative joint condition characterized by a progressive destruction of the articular cartilage leading to pain and functional loss, with knee OA being the most frequent type (1). Articular cartilage is a nonvascularized and noninnervated connective tissue that can go through many changes following microtrauma or age-related modifications (2). Because of their limited proliferative ability, articular chondrocytes have limited capacity for self-repair. Even minor injuries may progress to significant joint degeneration (3,4). The chondrocyte is therefore the cornerstone of cartilage regeneration and OA treatment.

Several lines of curative treatment options have recently been explored for OA, including surgery, but they are invasive and have shown varying efficacy (5). Conservative

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treatments include oral nonsteroidal antiinflammatory drugs (NSAIDs) and intra-articular (IA) administration of NSAIDs or hyaluronic acid. However, these treatments have shown no curative effect on inflammation in this condition (6).

New curative perspectives have appeared regarding cartilage regeneration. Cell therapy appears promising with the use of mesenchymal stem cells (MSCs), which are multipotent stromal cells that can differentiate in chondrocytes (7–10). Platelet-rich plasma (PRP) is plasma with a platelet concentration three to eight times higher than in blood, which permits the availability of higher concentrations of active growth factors and might improve the quality of cartilage repair, as suggested in human and animal models (11–13).

A previous study showed that MSCs activated by PRP can differentiate themselves in chondrocytes, which may have curative effect (14). Other recent studies (15–17) confirmed the safety of MSC and PRP percutaneous injections. In 2015, Campbell et al (18) showed potential symptomatic improvement with IA injection of PRP in knee OA. The aim of the present study was to assess the feasibility and safety of IA injection of MSCs and PRP together to treat patellofemoral OA, with magnetic resonance (MR) imaging and long-term clinical follow-up.

MATERIALS AND METHODS

Patients

This single-center prospective, descriptive cohort study was conducted from May 2013 to January 2014 in 19 consecutive patients referred to a single institution by sport medicine and orthopedic wards with persistent and symptomatic anterior OA knee pain to be treated with IA injection of MSCs and PRP after failure of initial conservative treatment. Patients gave their written consent. The study was brought to the French ethical board "Comité de Protection des Personnes" (registration no. DC2013/15) and registered with the "Agence Nationale de Sécurité du Médicament" (registration no. 2013-A01237-38).

Inclusion criteria were persistent symptomatic patellofemoral OA with normal radiographs and pathologic MR images and age greater than 20 and less than 60 years. Exclusion criteria were pregnancy, infections, previous corticosteroid injection of the knee, and immunodeficiency. Patients who received additional treatment after MSC and PRP injection during follow-up (medical or surgical) were also excluded from long-term follow-up assessment.

Clinical data assessment at month 0, before MSC and PRP treatment, was performed by using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for lower limbs (19). Used to assess pain, stiffness, and physical function, this test comprises 24 items divided into three subscales: pain (5 items), stiffness (2 items), and physical functions (17 items).

The present study included 10 men and 9 women (mean age, 43.1 y; median, 45 y; range 27–57 y). The mean duration of pain was 12 months (median, 11 mo; range, 7–19 mo). One patient (5.2%) left the study before early MR and clinical follow-up, and 3 (15.8%) left before 12-month clinical follow-up.

MR Data before MSC/PRP Treatment and MSC/PRP Preparation

Before IA MSC and PRP injection, all patients underwent an MR imaging evaluation by a senior musculoskeletal radiologist with at least 5 years of musculoskeletal imaging experience (B.D., A.S.) at month 0. During the MR imaging scan, patients were in supine position with full limb extension. All examinations were performed on a 1.5-T MR scanner. All examinations were performed between 3:00 PM and 5:00 PM, with identical room temperature (18°C), to overcome diurnal and temperature-linked variations of the cartilage (20). The conventional MR imaging protocol included sequences in **Table 1**. T2 mapping sequences were assessed on a workstation (GE Medical Systems, Waukesha, Wisconsin) with software dedicated to T2 mapping. All MR images were anonymized.

Two musculoskeletal radiologists (J.P., with 2 y experience, and B.D., with 5 y experience) analyzed the images in consensus, in random patient order, blinded to clinical data, and reported their results by using a prewritten reading grid. The patellofemoral cartilage was divided into 6 compartments in the axial view (**Fig 1**). For each chondral lesion, the radiologist recorded the associated joint compartment,

Table 1. MR Imaging Parameters

Sequence	Parameters
Sagittal T1-weighted	TR = 588 ms, TE minimum, Nex = 1, FOV 16 cm, thickness 3 mm, spacing 0.5 mm, 24 slices, anteroposterior direction, duration 2 min 17 s
Sagittal PDW	TR/TE, 2,362/45 ms; Nex = 2, FOV 16 cm, 3 mm thickness, 0.5 spacing, 24 slices, duration 3 min 14 s
Coronal PDW	TR/TE, 2,000/45 ms; Nex = 2, FOV 16 cm, 3 mm thickness, 0.5 spacing, 20 slices, duration 2 min 44
Axial PDW	TR/TE, 2,257/45 ms; Nex = 2, FOV 16 cm, 3 mm thickness, 0.5 spacing, 24 slices, duration 3 min 05 s
Axial T2 mapping sequence for patellofemoral joint	TR = 1,000 ms, TE = 6.1, 14.1, 22.1, 30.1, 38.1,46.1, 54.1, and 62.1 ms; Nex = 2; FOV 16 cm; 256 × 192 matrix; 9 slices; thickness = 3 mm with 0.6-mm spacing; duration 5 min 09 s

Note–MR imaging protocol comprised sequences included in standard protocol and T2 mapping.
FOV = field of view; Nex = number of excitations; PDW = proton density-weighted; TE = echo time; TR = repetition time.