LIPO-STEM

ADIPOSE TISSUE MSCs PURIFICATION KIT

ADIPOSE-DERIVED MESENCHYMAL STEM CELLS INJECTION IN KNEE OSTEOARTHRITIS: A CASE REPORT.

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Introduction

Osteoarthritis (OA) is one of the leading causes of disability in the elderly population worldwide[1]. The knee is the most affected joint, with a global prevalence of knee OA of 3.8%, accounting for more than 250 million cases[2-3].

Since replacement surgery can be a premature solution for early knee OA, several conservative treatment approaches have been developed, often by combining several treatment options. These include physical therapy, pharmacologic management (topic or oral NSAIDs, opioids, oral supplements as vitamin D, collagens, methylsulfonylmethane, curcumin, ginger), intra-articular injections (glucocorticoids, hyaluronic acid, platelet-rich autologous plasma) and minimally invasive surgery (arthroscopic debridement, autologous chondrocyte implantation). Some of these approaches have proven ineffective, others can temporarily reduce symptoms, but have limited or null effects in regenerating cartilage [4-5].

Intra-articular injections of Mesenchymal Stem Cells (MSCs) have been studied in the recent years, as a promising therapeutic tool to treat mild to moderate OA. In fact, MSCs can differentiate into chondrocytes and secrete bioactive molecules, having anti-inflammatory, lubricating, angiogenic, antiapoptotic, antifibrotic effects in the receiving site, thus improving symptoms and functional status[4,6].

Adipose tissue is an abundant source of MSCs (Adipose-derived MSCs (ADSCs)), its harvest is easy, inexpensive and fast, can be performed in a single-stage procedure with the following intra-articular injection, and no adverse events have been reported[7,8].

We present a case of knee OA treated with ADSCs processed with a new device: **Lipo-Stem™ (Biopsybell s.r.l., Mirandola (MO), Italy).**

Patient's history

The patient, an 84-year-old woman with no comorbidities, had suffered progressive left knee pain for about 2 years, increasing when flexing the knee in common daily activities, such as walking, climbing stairs or rising from sitting. Conservative therapy (oral NSAIDs, Hyaluronic intra-articular injections) had previously failed, partially reducing the pain for just a few weeks.

Physical examination revealed articular effusion, limited and painful mobility and articular crepitation.

X-ray *(fig. 1)* and Magnetic Resonance Imaging ***(fig. 2)*** showed a moderate knee OA (chondropathy, osteophytes, reduction of the femoro-tibial space, a torn medial meniscus and a moderate effusion).

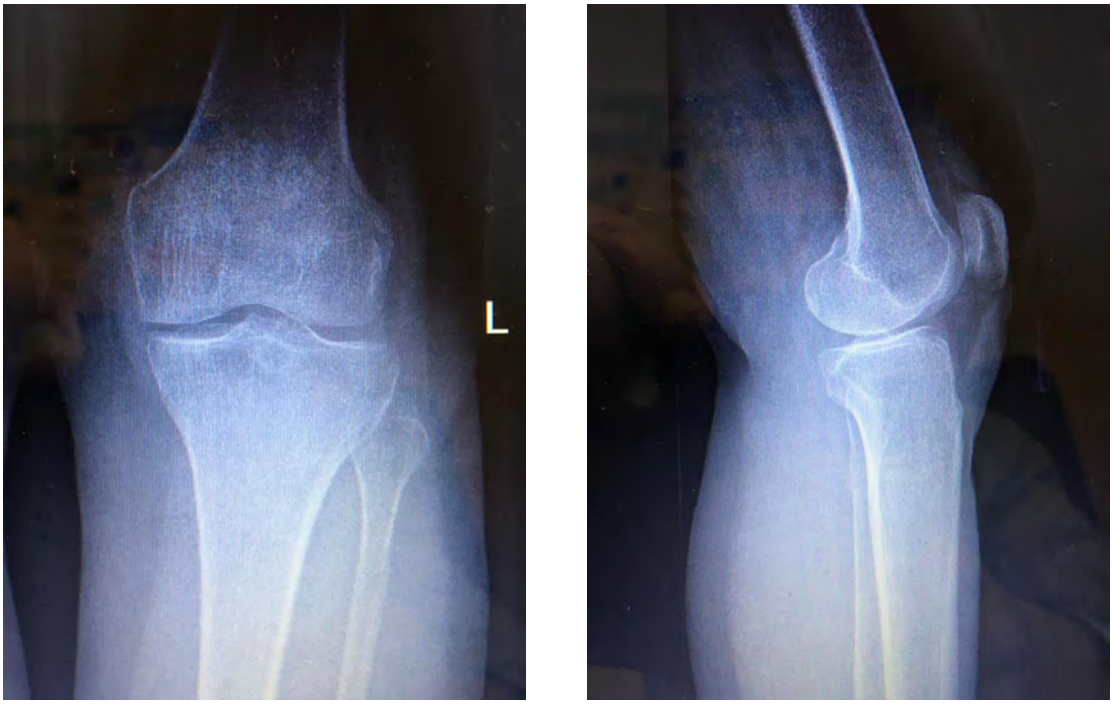

Figure 1. Pre-operative X-Ray of patient's left knee.

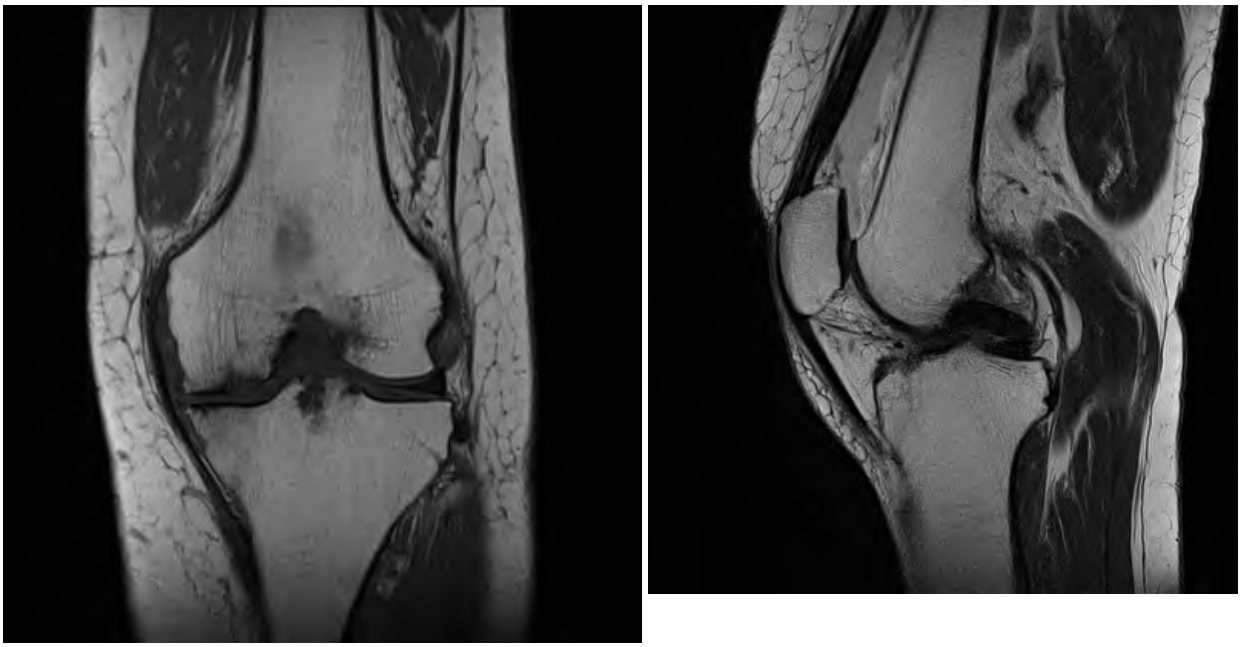

Figure 2. Pre-operative MRI image of patient's left knee.

Material and methods

Given the patient's age and the moderate severity of OA, surgery was excluded and we decided to perform a minimally invasive therapy: intra-articular injection of ADSCs processed with **Lipo-Stem™ (Biopsybell s.r.l., Mirandola (MO), Italy).**

This is a single-use kit intended for aspiration, processing and grafting autologous adipose tissue, packed in a sterilized box containing all the components needed for the procedure. The kit *(fig. 3)* includes different sizes of syringes for adipose tissue klein solution infiltration, adipose tissue liposuction and for fat injection, metal blunt cannulas for adipose tissue klein solution infiltration (16 G Ø) and lipoaspiration (13 G Ø), a 16 G grafting needle, a filter bag for adipose tissue microfragmenting and washing, a drip chamber with tip to perforate the bag of saline solution with clamp, a waste collection bag.

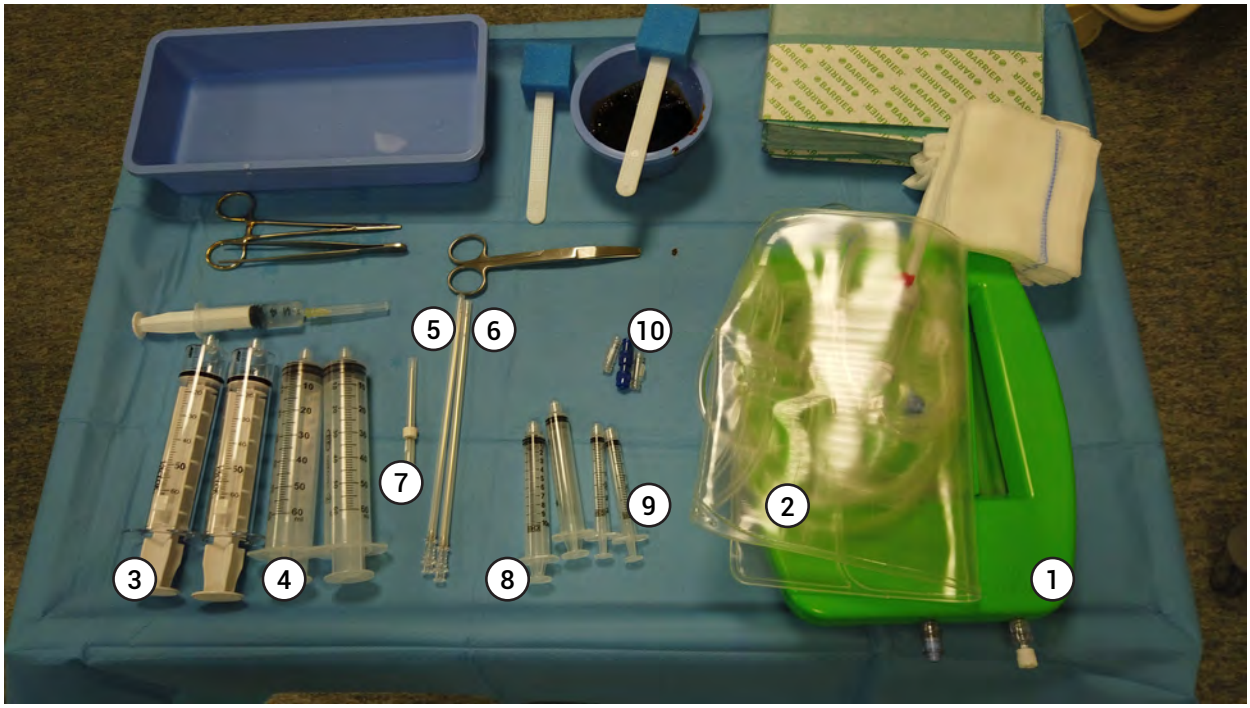

Figure 3. Surgery kit: Lipo-Stem kit, local anaesthetic syringe, Klein solution bowl, anchillary surgical instruments.

STANDARD KIT COMPOSITION:

1. Lipo-Stem™ system with filtering bag
2. Waste bag and Infusion with clamp
3. VacLok syringes 60ml
4. Syringes 60ml
5. Klein cannula 16G
6. Lipo-aspiration cannula 13G
7. Infiltration needle 16G x 50mm
8. Syringes 10ml
9. Syringes 3ml
10. Combi caps LLF/LLM and Luer connectors LLF/LLF

In the operating room, the patient was placed in supine position and antibiotic prophylaxis was intravenously administered (Ceftriaxone 1g). After scrubbing with a iodopovidone-based solution and draping, the abdomen was chosen as donor site for the adipose tissue.

Figure 4. Klein solution infiltration in the subcutaneous adbominal tissue.

Through a 2-3 mm cutaneous incision made under local anaesthesia (1 cc of a 2% Lidocaine), the subcutaneous abdominal tissue was infiltrated with 150 ml of Klein solution *(fig. 4)*:

- 20 ml of 2% lidocaine
- 0.25 cc of 1 mg/ml adrenaline
- 2 cc of sodium bicarbonate
- 250 ml of 0.9% saline solution

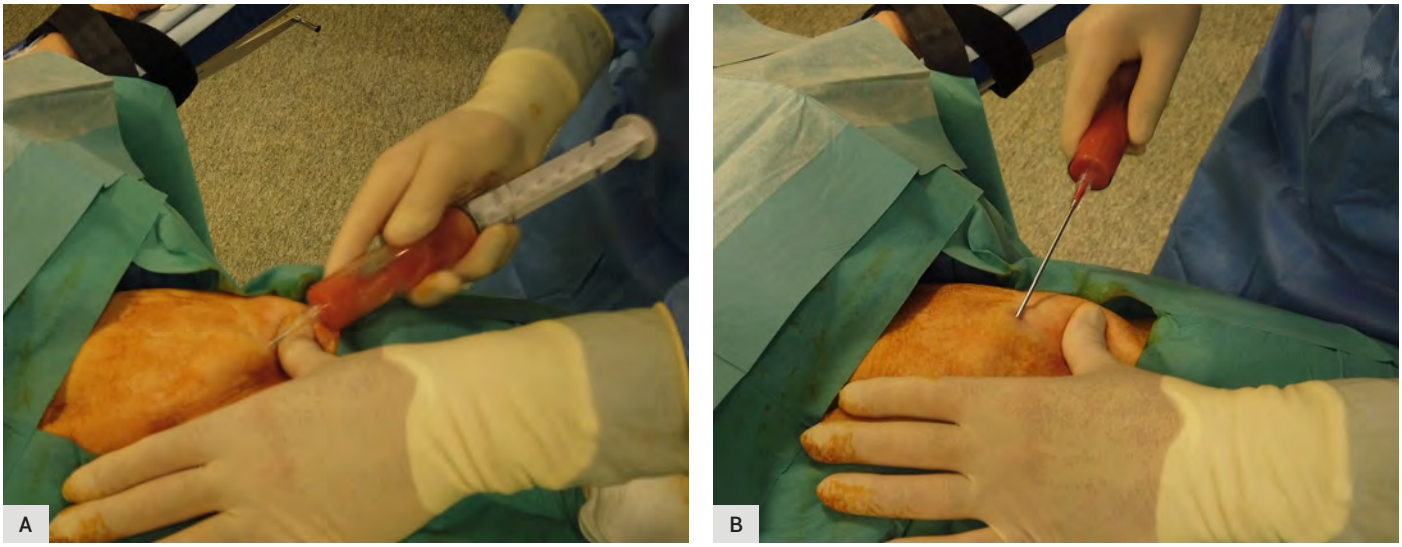

Figure 5. Lipoaspiration in the previously inflitrated area.

After 7-10 minutes, about 30 cc of adipose tissue were harvested through a wet liposuction technique *(fig. 5-6)*. The abdominal incision was closed with a thin bandage, and an adhesive foam pad was applied on the treated area.

Figure 6. Harvested adipose tissue before the microfragmentation and purification process.

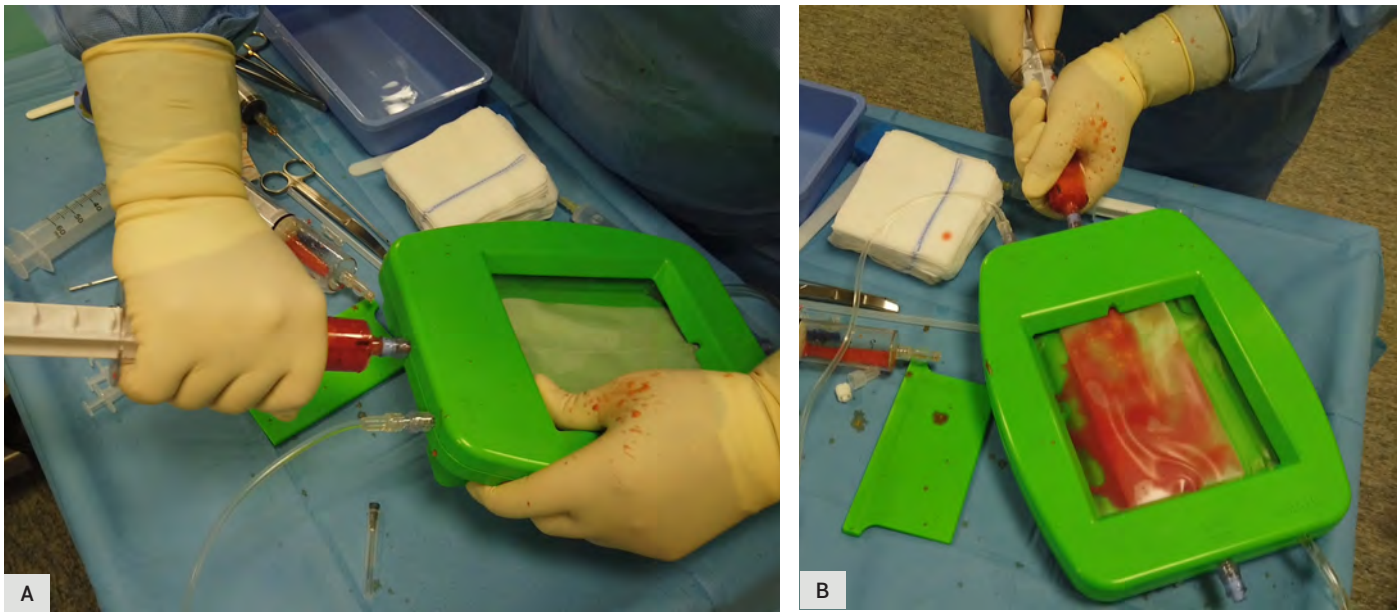

Figure 7. Lipoaspiration syringe connection to the device's LIPO-IN valve (A) and transfer into the Lipo-Stem processing bag.

The collected tissue was immediately processed with the **Lipo-Stem™** device. The liposuction syringe was connected to the device's LIPO-IN valve *(fig. 7A)* and the adipose tissue was transferred to the filter bag *(fig. 7B)*.

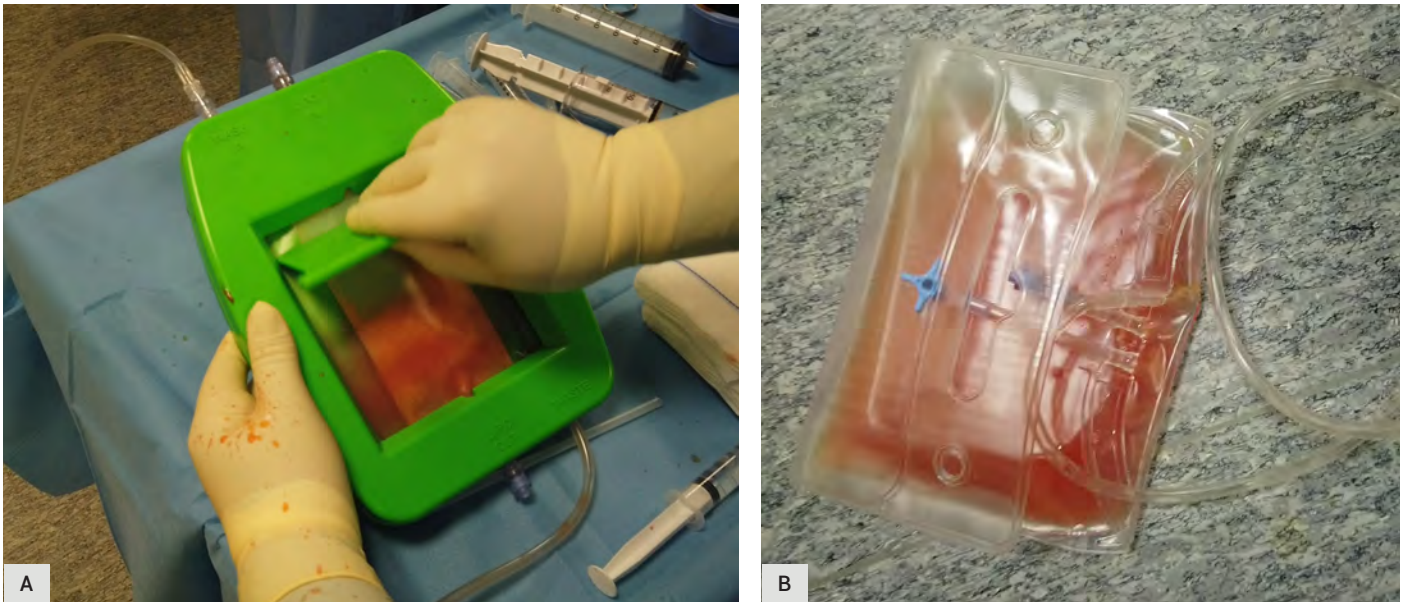

Figure 8. Adipose tissue processing phase: microfragmentation and purification (A) from all pro-inflammatory residues, which are discharged in the waste bag (B).

Following the manufacturer's instruction, the tissue underwent a delicate and fast mechanical processing in a continuous saline solution washing *(fig. 8-A)*: the clusters of adipose tissue were reduced in size, while the blood components with pro-inflammatory properties and the oily substances were washed away and eliminated through the waste bag connected to the bottom of the filtering box *(fig. 8-B)*.

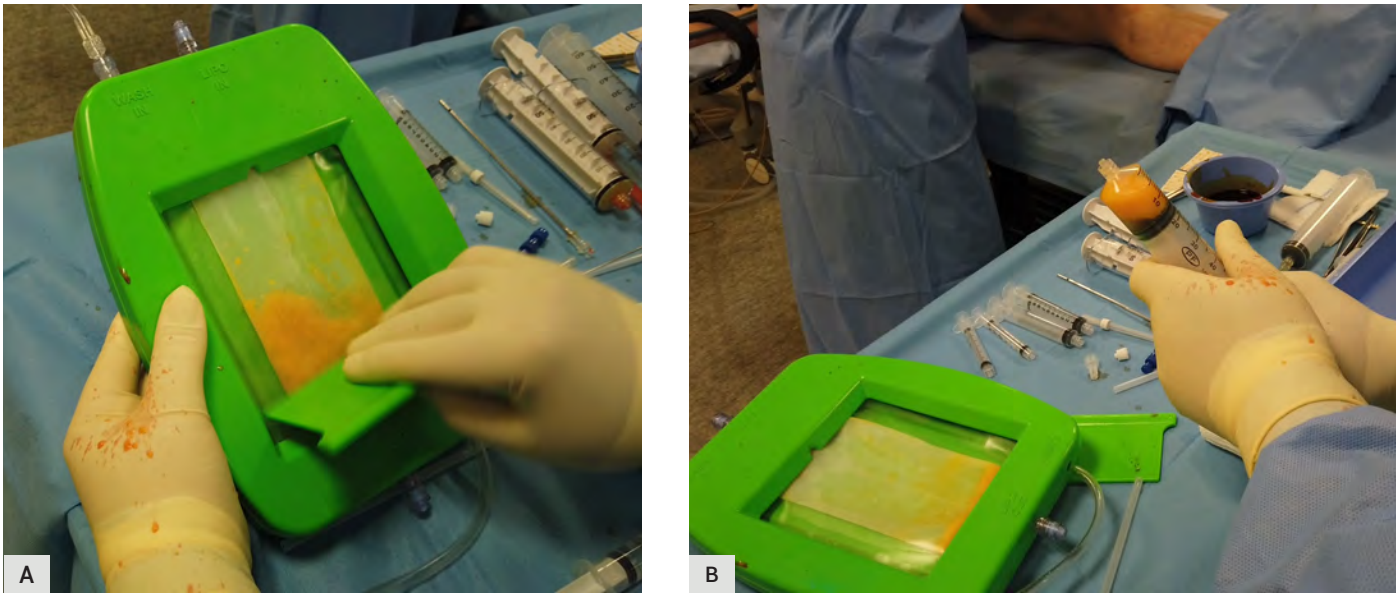

Figure 9. Adipose tissue processing phase: the resulting product.

In about 5 minutes, we obtained 7 cc of microfragmented micronized adipose tissue product *(fig. 9)*, which was injected intra-articularly in the left knee *(fig. 10)*, kept in flexion position, after cutaneous infiltration with 1 cc of 2% lidocaine, through a lateral access. The injection point was medicated with sterile dressing.

Figure 10. Processed adipose tissue intra-articular reinjection in the left knee.

Results

The procedure was painless, just a mild and brief discomfort was perceived by the patient during the intra-articular injection, and she referred the knee pain totally ceasing immediately after the injection. The articular crepitation when flexing the knee was no longer detectable as well. The patient was discharged 30 minutes after the procedure with paracetamol 1000 mg if needed, and with the indication to avoid efforts, but with permission to weightbearing.

The post-operative course was uneventful and the patient was very satisfied for being able to return to her normal life soon after.

Outpatient controls were made at 1,3 and 6 months postoperatively. In this timeframe physical examination was unremarkable and the patient referred an almost complete resolution of the algic symptoms, with no need for any further pharmacological or physical therapy.

Discussion

Knee OA is a chronic inflammatory disease responsible of an increasing number of disabilities and social costs worldwide[1-3]. Since surgery does not always reduce the pain and is recommended only in severe cases, a lot of different conservative therapies have been developed over time, aiming at reducing the symptoms and delaying disease progression[9]. Among these treatments, the intra-articular injection of MSCs is gaining increasing attention[10].

MSCs are multipotent cells with the ability to differentiate into various tissues (bone, tendon, articular cartilage), and having trophic, anti-scarring, immunomodulatory, mitogenic, anti-apoptotic and anti-microbial properties, due to their production of growth factors, bioactive elements and cytokines that detect and signal changes in the microenvironment where they reside[11]. Perivascular cells or perycites, have been reported as the progenitors of MSCs[12]. Perycites and MSCs can be found in the extracellular matrix of various tissues, mainly the bone marrow and, more abundantly, in the adipose tissue. This is an ideal donor site because of its easier access, a much reduced donor site morbidity, and its richness of vascular niches, thus representing an important source of potential healing and regenerative pericytes and ADSCs[13].

Intra-articular injections of autologous fat tissue in patients with knee OA have shown promising results in several studies[10], providing volume, cushioning, support and having potential healing and regenerative capabilities[14]. A recent systematic review has shown higher clinical and imaging scores in patients treated with ADSCs, with clinical improvement maintained up to 1 year and evidence of regenerated hyaline cartilage[13]. However, studies on MSCs intra-articular injection are heterogeneous and standardized protocols for tissue collection and processing are lacking[10].

Lipo-Stem™ is a new device, allowing to process adipose tissue from a normal liposuction and obtain a micro-fragmented, micronized product, ready for autologous injection in the affected joints in one operating stage, with no need for laboratory manipulation (enzymatic processing, haemolysis, culturing), thus greatly reducing the preparation time and avoiding higher costs, ethical issues and regulatory constraints.

Fat tissue can be easily and rapidly harvested from the abdomen or hip/thigh regions, with minimal donor-site morbidity. While the donor region is being dressed, the lipoaspirate undergoes a rapid, delicate and easy mechanical processing and is reduced in size through a system of filters and a continuous saline solution washing that eliminates blood residues with pro-inflammatory properties, and the final product is ready to be injected immediately.

In our case, both the liposuction and the intra-articular injection were performed under local anesthesia in less than 1 hour, the patient reported just a little discomfort during the injection, but she had an instant pain relief at her knee and she was able to go home with no contraindications to weightbearing. No adverse events were observed, and the patient was very satisfied of the significant and prolonged improvement in pain control, functional status and quality of life, with no need for pharmacological therapy up to 6 months post-treatment.

Conclusions

Although literature lacks well designed and comparative standardized studies, autologous micronized fat injections represent a promising treatment option in OA. Albeit this is a single case report, part of a larger ongoing study, the results are very encouraging and **Lipo-Stem™** appears to be a very handful, safe and effective device for the conservative treatment of mild to moderate OA or in patients not responsive to other current treatments.

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