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The treatment of chondral lesions of the knee with the microfracture technique and platelet-rich plasma

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Abstract

Purpose: to assess the efficacy of associating the microfracture technique with platelet-rich plasma (PRP) injections in the treatment of chondral lesions to promote acceleration and optimization of the healing process compared with the traditional microfracture approach.
Methods: from September 2011 to August 2012, 20 patients (9 males and 11 females, aged 30-55 years) were treated. All presented with chondral lesions of the medial femoral condyle of the knee and a pain duration ranging from 8 to 12 months.
The patients were randomized into two groups (A and B). Group A was treated with the microfracture technique and a total of three intra-articular injections of PRP. Group B was treated with microfractures alone. Clinical follow-up was performed at 3, 6 and 12 months after treatment. Clinical function was assessed on the basis of the International Knee Documentation Committee (IKDC) score. Pain was evaluated using a visual analogue scale (VAS).
Results: the patients in group A had a mean baseline IKDC score of 31.2, which rose to 84.2 at 12 months. The IKDC scores in group B were at 30.1 at baseline and 81 at 12 months.
Conclusions: the results of our study suggest that functional recovery and resolution of pain are obtained more quickly in PRP-treated patients. We also observed a better functional outcome in the patients treated with the combination of PRP and microfractures, even at 12 months, although the difference was not statistically significant.
Level of evidence: level II, randomized clinical study.

Key Words: chondral lesions, cartilage regeneration, microfracture, platelet-rich plasma.

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Introduction

An isolated chondral lesion, even small, is sufficient to modify the joint environment. The past decade in particular has seen an increase in the frequency of this type of pathology. This is linked to a trend of growing participation in sports, but also to an increased emphasis on, and cultural awareness of, the importance of physical activity across all age groups. People today are therefore more active than previous generations, but, paradoxically, they are sometimes markedly overweight. A cartilage injury that is not properly treated, especially in young people, can evolve into degenerative osteoarthritis (OA) and may become a main cause of impaired joint function and reduced quality of life. These considerations are driving scientific research efforts to identify novel chondral regeneration techniques for treating these lesions. However, among the techniques introduced to date, none has proved to be superior to the others in terms of promoting hyaline cartilage regeneration and ensuring maintenance of the results obtained.
The microfracture technique was introduced into surgical practice more than twenty years ago, and its use is supported not only by this long experience, but also by many surveys that have assessed its effectiveness, and specified the indications for treatment with this approach. Its limitations are also well known, in particular the fact that the lesion is repaired with fibrocartilage and the poor maintenance of outcome in the long term (1-5).
Platelet-rich plasma (PRP) is thought to stimulate the

proliferation of chondrocytes and the differentiation of mesenchymal cells of the subchondral bone into the chondrogenic line. This is the rationale underlying our decision to combine the use of microfractures with PRP injections; PRP is also thought to have an anti-inflammatory action on the synovial membrane, promoting early clinical improvement (6-10). It is current opinion that the progression of joint degeneration is due to a loss of the balance between pro-inflammatory cytokines (including IL-1 alpha, IL-1beta, tumor necrosis factor-alpha) and inflammatory cytokines (IL-4, IL-10, IL-1ra). This cytokine imbalance is thought to activate proteolytic enzymes, thus leading to cartilage destruction (7). It is suggested that PRP might restore the balance of cytokine-mediated homeostatic mechanisms, blocking the articular degenerative processes (11).

The purpose of the present study was to assess the validity of the association of the microfracture technique and intra-articular PRP injections in the treatment of chondral lesions of the knee. The hypothesis of the study was that microfractures combined with PRP can improve clinical outcome compared with traditional microfracture treatment alone.

Methods

Patients with Outerbridge grade 2-3 chondral lesions of the medial femoral condyle of the knee were included in this study. Exclusion criteria were: combined meniscus and/or ligament injuries, previous failed surgical treatment of the chondral defect, limb malalignment, a body mass index (BMI) greater than 30, and the presence of comorbidities, such as inflammatory arthritis, metabolic diseases, and local or systemic infectious diseases.

The patients were randomized into two groups (A and B). Group A was treated with the microfracture technique and articular injections of PRP. Group B was treated with microfractures alone.

Microfractures were performed as recommended in the literature (12). All the damaged cartilage was removed in order to obtain stable lesion margins, surrounded by healthy cartilage, and perfectly perpendicular borders. This is necessary in order to allow the clots to adhere in a stable manner to the bottom of the lesion and to reduce the direct load on the lesion, thereby allowing a better repair. During the procedure, particular care was taken to protect the subchondral bone. The holes in the subchondral bone were drilled in a centripetal direction, from the margins to the center of the lesion; they were spaced 3-4 mm apart and drilled to a depth of about 4-5 mm, so as to ensure penetration of the medullary cavity; achievement of the correct depth was confirmed by arthroscopic visualization of fat droplets in the joint after drilling (12).

The PRP infiltration protocol was a cycle of three intra-articular injections of autologous PRP. The first was performed one week after surgery, while the second and the third were each performed at an interval of one month from the previous one. The GPS system II (Biomet Biologics, Warsaw, IN, USA) was used to obtain platelet concentration. The procedure involves drawing peripheral venous blood (30cc) using a syringe pre-treated with Anticoagulant Citrate Dextrose Solution Formula - A (ACDA) in a blood: ACDA ratio of 10:1. The blood sample is placed in a particular filter device (GPS II) and then centrifuged (3200 g for 15 min) to separate the different plasma fractions. This results in isolation of the platelet concentrate, which is equal to around 10% of the volume of blood taken (3 cc in this case). Two precautions were taken when performing the infiltration: 1) we used use of a needle with a caliber 22 gauge in order to prevent lysis and therefore early activation of the platelets; 2) we added about 50-150 microns of sodium bicarbonate to the PRP (to reach a proportion of 8.4%) in order to optimize the effect of pH on the platelet activity.

Both groups underwent the same rehabilitation program, which included: early mobilization, especially after the infiltration of PRP to facilitate its intra-articular diffusion; early continuous passive motion; isometric and isotonic exercises; deambulation with 50% load using crutches for 10 days, followed by gradual increments depending on the muscle trophism and the joint response (effusion); full loading at 20 days in the presence of good muscle tone. Under no circumstances were immobilization devices, physical therapy and chondroprotective drugs used.

Clinical follow-up was performed at 6 and 12 months after treatment, always integrating the functional evaluation with a clinical examination, recording the International Knee Documentation Committee (IKDC) score, and measuring pain with a VAS scale.

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Results

In the period between September 2011 and August 2012 we enrolled 20 patients (9 males and 11 females) aged between 30 and 55 years. The duration of their pain symptoms ranged from 8 to 12 months. The IKDC scores of the single patients, randomized to the two groups, are reported in **Tables 1** and **2**. In group A, the mean IKDC score was 31.2 ± 4.6 at the baseline evaluation, 65.6 ± 11.5 at six months, and 85.8 ± 6.9 at 12 months. In group B, the mean IKDC score was 30.1 ± 4.6 at baseline, 52.4 ± 9.8 at 6 months, and 74.3 ± 5.3 at 12 months. The difference between the two groups was not significant at the baseline evaluation. At both the 6-month and the 12-month follow-up evaluation, the mean IKDC score of group A was significantly higher than that of group B (p-values of 0.013 and 0.001, respectively).

The VAS scores recorded in the two groups are listed in **Tables 3** and **4**. In group A the mean VAS score was 8.2 ± 0.6 at baseline, 5.7 ±0.8 at 6 months, and 1.4 at 12 months. In group B the mean VAS score was 8.1 ± 0.6 at baseline, 6.2 ± 0.8 at 6 months, and 2 ± 0.7 at 12 months. The difference between the two groups was not significant at any evaluation (p-values of 0.714, 0.182 and 0.126 at baseline, 6 months and 12 months, respectively).

Discussion

The treatment of cartilage lesions continues to be a challenge for the orthopedic surgeon, with the available surgical options being found to produce less than optimal results. This has led to the search for biological supports able to enhance cartilage repair, including PRP, which, in the form of intra-articular injections, has also been investigated for the treatment of OA (6-11). The recently proposed association of microfractures with PRP has already shown promising results in animal models (13) and started to receive confirmation in humans, as demonstrated by our study. The microfracture technique, introduced by Steadman in 1980 (14), is still often the first-line of treatment for chondral lesions. The use of microfractures rests on a basic principle, namely that of stimulating the bone

Table 1 - IKDC scores of group A, treated with the microfracture technique and platelet-rich plasma.

Patient	Preoperative (baseline)	6 months	12 months
1	39.1	69.3	88.5
2	31	50.9	76
3	25.3	48.9	72.8
4	36.8	54.1	87.4
5	33.3	60.3	85.1
6	32.2	75	96.4
7	25.6	70	85.3
8	31	79	87.4
9	26.1	81	92
10	31.8	67.9	86.8

Table 2. IKDC scores of group B, treated with microfractures alone.

Patient	Preoperative (baseline)	6 months	12 months
1	31.9	65.8	84.8
2	32.8	40.8	73.5
3	33.1	58.9	81.8
4	26.2	45	69.8
5	29.4	52	73
6	33.9	44.6	72
7	30.5	66.9	76.9
8	28.3	57.9	70.2
9	27.9	40.1	71.8
10	27.3	51.7	69.1

Table 3. VAS scores of group A, treated with the microfracture technique and platelet-rich plasma.

Patient	Preoperative (baseline)	6 months	12 months
1	7	5	1
2	8	6	2
3	9	7	3
4	8	6	2
5	8	7	1
6	9	5	0
7	8	6	2
8	8	5	0
9	9	5	2
10	8	5	1

Table 4. VAS scores of group B, treated with the microfractures alone.

Patient	Preoperative (baseline)	6 months	12 months
1	9	7	3
2	8	6	2
3	8	5	1
4	8	7	2
5	7	5	1
6	8	6	2
7	8	6	2
8	9	7	3
9	8	6	2
10	8	7	2

marrow through penetration of the subchondral bone plate and subsequent recruitment of mesenchymal stem cells for chondral repair (14). The strengths of this technique are its speed and simplicity of execution and its low costs. Furthermore, adverse events related to microfractures are very rare, confirming the excellent safety profile of the procedure (1-5). Its main disadvantage, however, is the fact that the lesion is repaired with fibrocartilage, which impacts on the joint's ability to absorb mechanical load. Indeed, fibrocartilage contains more collagen and less proteoglycans than normal intra-articular hyaline cartilage, and a much greater concentration of type I compared with type II collagen. It is well known that type I collagen shows less resistance to compression, elasticity and wear compared with type II (15). Furthermore, while hyaline cartilage is normally subjected to load in compression, fibrocartilage is normally subjected to load in tension, which means that the latter is not biomechanically suited to serve as articular cartilage. In fact, repeated mechanical stresses can eventually lead to failure of a fibrocartilage repair. It has been shown that the initial benefit of microfractures tends to decrease between 18 and 36 months after the procedure, however, despite this deterioration, the postoperative functional scores remain higher than those recorded preoperatively (16). From these considerations it is clear that the use of platelet growth factors, able to induce improvement of the biological environment, could play a crucial role in improving the quality of chondrogenesis. PRP is believed to exert its effect through direct stimulation of chondrocytes and mesenchymal stem cells of the subchondral bone and, especially in the early stages, through a direct anti-inflammatory action in the synovial membrane (11). From a histological perspective, neovascularization, potentially induced by platelet growth factors, does not appear to play a useful role, given the avascular nature of cartilage tissue. The results of our study suggest that functional recovery and resolution of pain are obtained more quickly in PRP-treated patients. The results also showed a better functional outcome (based on the IKDC score) in the patients treated with the combination of PRP and microfractures, even at 12 months, although the difference was not statistically significant. In order to increase the significance of this study we aim to extend the follow-up of the treated patients, in order to assess long-term maintenance of the outcome.

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