THE CLINICAL EFFECT OF INTRAARTICULAR INJECTIONS OF AUTOLOGOUS PLATELET-RICH PLASMA AS AN AUGMENTATION PROCEDURE AFTER SURGERY FOR PATIENTS WITH CONDROPATHY OF THE KNEE – CASE SERIES

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Abstract: *The aim of the study was to investigate whether platelet-rich plasma (PRP) application after arthroscopic microfracture procedure for condropathy of the knee is associated with improved clinical outcome. Materials and Methods: We enrolled prospectively 41 patients treated with microfracture procedure for condropathy of the knee. 23 received postoperative 3 intraarticular injections of PRP at 2-weeks intervals. The clinical outcome was evaluated using Knee Injury and Osteoarthritis Outcome Score (KOOS) and International Knee Documentation Committee Subjective Knee Form (IKDC), recorded at 3 and 6 months. Results: At 3 months KOOS improved significant in PRP group (p<0.001), but the difference was not maintained at 6 months (p=0.097). At 3 months IKDC improved significant in PRP group (p=0.002) and the difference was maintained at 6 months (p=0.001). Conclusion: PRP may accelerate the healing process in patients treated with microfracture procedure for condropathy of the knee but there might be no difference in the final outcome.*

INTRODUCTION

Hyaline cartilage protects the underlying bone from excessive load and trauma by dissipating the forces produced during movement.(1) Due to its poor blood supply and self-renewal capacity, the normal structure and function of cartilage are difficult to restore when it is injured or degenerated. Patients with articular cartilage injuries, if untreated may go on to develop early onset osteoarthritis with long term morbidity and consequent high use of health service resources.

In the last years a completely new approach for the treatment of cartilage lesions has developed based on biological strategies. The modern therapeutically approach includes: application of matrix metalloproteinase inhibitors, gene therapy, cytokinase inhibitors, stem cells and growth factors.(2) These approaches are based on the revolutionary idea of "regeneration" unlike the traditional approach focusing on the concept of "repair".(3-5) The biological rational behind this treatment is the topical administration of several important molecules normally involved in joint homeostasis, healing mechanism and tissue regeneration.(6) Growth factor effects have been evaluated extensively both in vivo and in vitro (7-9) and they were proved to have a potential beneficial effect in promoting cellular anabolism and tissue regeneration. Platelet-derived growth factors play important roles in the regulation of growth and development of several tissues, including cartilage.

Platelet-rich plasma (PRP) with higher platelet concentrations than the mean blood measures is one of the sources for growth factors (10) and represents one therapeutic application with promising preliminary clinical results.(11-13) Platelets contain significant amounts of cytokines and growth factors.(14) The local concentration of these factors might stimulate cell proliferation, chemotaxis, migration, cellular differentiation and extracellular matrix synthesis in the process of restoration of the cartilage lesions.(1,15,16)

PRP can be defined as the volume of the plasma fraction from autologous blood with a platelet concentration above baseline count (200 000 platelets/μL) (17) even if in the literature, PRP concentrations have been reported to range widely, up to 8 times that of basal levels.(18)

PURPOSE

The purpose of this study was to investigate whether platelet-rich plasma application as an augmentation procedure after arthroscopic microfracture procedure for patients with condropathy of the knee is associated with improved clinical outcome compared with traditional microfracture treatment alone.

MATERIALS AND METHODS

We enrolled prospectively a number of 41 patients treated with arthroscopic microfracture procedure for condropathy of the knee, admitted in the Orthopedics Clinics No. I of the Clinical County Emergency Hospital Mureş, between October 2012 and March 2014. Our including criteria were: patients with ICRS grade 3 and 4 chondral lesions of the medial femoral condyle with the defect size <2 cm2 of the knee that underwent surgical intervention of arthroscopic microfracture procedure.

Exclusion criteria were: limb malalignment, a body mass index (BMI) greater than 30, the presence of comorbidities such as inflammatory arthritis, autoimmune and platelet disorders, local or systemic infectious diseases, history of knee articular injections of corticosteroids during previous 3 weeks or use of systemic corticosteroids 2 weeks before PRP injections, and platelet counts of less than normal value (150 000 per microliter).

Microfractures were performed as recommended in the literature.(19) First the area undergoing microfracture is prepared by removing any loose or damaged cartilage in order to obtain stable lesion margins. The calcified cartilage layer was

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removed to expose the subcondral bone. Multiple holes were made in the exposed bone about 3 mm apart with a 1.1 mm K-wire and drilled to a depth of about 4-5 mm. By picking holes in the subchondral bone, blood and fat droplets (which contain stem cells) are given a pathway to flow into the defect or lesion. This develops in to a mesenchymal clot, which will mature and form in to fibrocartilage.

23 of these patients received postoperative, 3 intraarticular injections of autologous PRP (Platelet-Rich Plasma) at 2-week intervals. The first was performed one week after surgery. Standard blood investigations were done before treatment, including complete blood count and coagulation profile. The PRP development was done using the analogical centrifuge Nahita 2615. For preparing 4-6 mL of PRP, 15 mL of blood was first collected from the patient. The sample was centrifuged for 10 minutes at 4000 revolutions per minute. Subsequently, we obtained 4-6 mL of PRP, and we proceeded to the intra-articular infiltration by a parapatellar approach under sterile aseptic conditions. As the anesthetic agents might have toxic effects on chondrocytes and might change the pH of the environment influencing the activation of platelet (7), no local anesthetic agent was injected. Exogenous factor for the process of activation before injection was not used, but let the platelets be in contact directly with the joint collagen to become active (7) and to induce rapid fibrin clot formation. After 15–20 minutes of rest, patients were asked to actively flex and extend their knees so that the PRP could spread evenly across the joint space before changing into gel. Local ice application was recommended 20 minutes every 2 to 3 hours for 24 hours. In the case of pain onset, they had permission to use 1 gram of acetaminophen and if persistent, acetaminophen- tramadol hydrochloride could be used. Immobilization devices and chondroprotective drugs, NSAIDs, aspirin, or any steroids were prohibited.

Both groups underwent the same rehabilitation program: postoperative no weight bearing on the operated joint for 21 days. Meantime they were instructed with exercise therapy and activity of daily life modifications.

For all the patients included in the study, the clinical outcome (pain, function, and quality of life) was assessed using Knee Injury and Osteoarthritis Outcome Score (KOOS) and International Knee Documentation Committee Subjective Knee Form (IKDC), recorded prior to the surgical intervention and then at 3 and 6 months.

The Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaire is intended to monitor the short- and long-term consequences of any type of knee injury.(20)

The IKDC subjective is also a knee-specific instrument, developed to measure symptoms, function and sport activities in patients with a variety of knee problems. Although originally designed for the assessment of ligament disruption, the IKDC has been shown to provide a superior overall measure of disability when compared with the KOOS, in patients who have undergone cartilage regeneration procedures.(21)

RESULTS

The present study enroled a number of 41 patients (24 males and 17 females) treated with arthroscopic microfracture procedure for condropathy of the knee. Patients' age ranged 17-58 years, and the average was 38.49 ± 10.13 years.

The average preoperative KOOS score was: 60.72% ± 6.12 for patients without PRP injections and 63.22% ± 4.03 for patients receiving PRP injections (p=0.125). At 3 months KOOS score improved statistically significant for patients receiving PRP injections, with an average of 87.91% ± 2.08 compared to 83.89% ± 3.30 (p<0.001) for patients without PRP injections. But this statistical significant difference was not maintained at 6 months (p=0.097), with an average KOOS score of 91.94% ± 3.63 for patients without PRP injections and 93.57% ± 2.46 for patients receiving PRP injections.

Regarding the five subscales of the KOOS score at 3 months, we found a statistical significant difference (p<0.05) in three out of five subscales: pain, activities of daily living, sport and recreation function. At 6 months, although a trend favorable for the PRP group was noticed, we did not find a statistical significant difference in any of the five subscales of the KOOS score.

The average preoperative IKDC subjective score was: 47.06% ± 8.88 for patients without PRP injections and 48.17% ± 11.63 for patients receiving PRP injections (p=0.737). At 3 months IKDC subjective score improved statistically significant for patients receiving PRP injections, with an average of 73.70% ± 6.32 compared to 68.06% ± 4.20 (p=0.002) for patients without PRP injections. In case of this score the statistical significant difference was also maintained at 6 months (p=0.001), with an average IKDC subjective score of 85.33% ± 5.02 for patients without PRP injections and 90.09% ± 3.74 for patients receiving PRP injections.

DISCUSSIONS

The microfracture technique was introduced into surgical practice more than twenty years ago. Microfracture surgery of the knee is indicated to resurface well-defined, small to medium size areas of full-thickness articular cartilage damage of the knee. Its limitations are also well known, in particular the fact that the lesion is repaired with fibrocartilage, which lacks the biomechanical characteristics of hyaline cartilage that are necessary to withstand the forces distributed across the knee and the poor maintenance of outcome in the long term (initial benefit tends to decrease between 18 and 36 months after the procedure).(22-24)

The clinical efficacy of PRP treatment in various osteochondral pathologies is still under debate and standardized protocols have not yet been established. Intra-articular PRP injections could improve postoperative clinical outcome in these patients by improving the quality of chondrogenesis (25) and by reducing the inflammation and, subsequently, the pain at the surgical site.(26) Delivery of high concentrations of cytokines and growth factors to damaged tissues by PRP might modulate the proliferation of the mesenchymal stem cells of the bone marrow into the chondrogenic line.(25)

The association of microfractures with PRP has already shown promising results in animal models. Milano et al. (27), in an animal study, suggested that PRP showed a positive effect on cartilage restoration after microfracture, although none of their experimental treatments produced hyaline cartilage.

Our study showed that intraarticular injections of autologous PRP may accelerate the healing process in patients treated with arthroscopic microfracture procedure for condropathy of the knee, but there might be no significant difference in the final outcome.

Another recent published clinical study (25), which included 20 patients obtained results similar to ours. They suggested 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.

Promising effects were obtained in treating osteochondral talar lesion in the randomized, prospectively designed study of Guney et al.(28) They sustained that an immediate postoperative PRP injection may improve the functional recovery of talar osteochondral lesions treated by

microfracture technique at a medium term follow-up (average 16 months).

PRP has been also locally applied by means of scaffolds, following the principles of the acellular one-stage cartilage repair. Several preclinical evidences have shown a positive effect of PRP in association with different materials.(26,29)

To date, there is no consensus on the number of injections, the most effective platelet concentration, activation methods, injection intervals, the length of long-term PRP effects, nor eligible patient selection.(18) The platelet count is strictly linked to the procedures employed.

There are two main methods of PRP processing after centrifugation of whole blood: separation of the buffy coat layer or isolation of the plasma layer.(30) Buffy coat preparations are developed using high centrifuge spin rates for long durations, in order to retain the maximum number of platelets. These preparations also contain a higher concentration of leukocytes and some residual erythrocytes. Plasma-based products are prepared using a slower centrifugation rate over a shorter period of time so they contain fewer platelets. Compared to buffy coat preparations plasma-based products but are generally devoid of both white and red blood cells.(30)

In the second case, also the method used in the present study, several variables such as number of centrifugations, their speed and timing, might influence the final product in terms of concentration of different cellular types. PRP content also fluctuates from one patient to another and within the same patient at different time points leading to various in vivo effects.(31) The varying methods used for PRP production may be a cause for the different outcome observed in studies assessing the efficacy of PRP treatment.(30)

Limitations:

In our patients, we did not investigate the improvement of cartilage lesions utilizing magnetic resonance imaging and/or biopsy or immunology at final follow-up.

CONCLUSIONS

Intraarticular injections of autologous PRP may accelerate the healing process in patients treated with arthroscopic microfracture procedure for condropathy of the knee, but there might be no significant difference in the final outcome.

Although PRP seems to positively influence the cartilage repair process, further studies are needed to clarify some fundamental aspects such as the best PRP formulation, the best protocols of administration, and also the eligible patient and lesion selection.

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