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Original research

Using platelet-rich plasma to treat jumper's knees: Exploring the effect of a second closely-timed infiltration

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ABSTRACT

Objectives: Some clinical series have evaluated the effect of platelet-rich plasma (PRP) in the treatment of proximal patellar tendinopathy. Although it is possible that a single infiltrative administration may prove to be an effective treatment for this indication, most of the existing studies evaluated the effects of two or three successive infiltrations. The aim of this study was to evaluate whether two infiltrations of PRP proves more effective than a single treatment.
Design: Prospective, randomized and comparative study of level 2.
Methods: Twenty patients suffering from chronic proximal patellar tendinopathy were enrolled into the study and split into two randomized groups (one or two infiltrations of PRP, respectively). The 3-month follow-up evaluation consisted of VAS, IKDC and VISA-P scores, along with algometer, isokinetic and ultrasounds evaluations. After 1 year, subjects were contacted to define their functional evolution.
Results: The concentration of the PRP used for each infiltration was similar in both groups, and contained no red or white cells. Results revealed no difference in treatment efficacy between the groups.
Conclusions: The comparison between one or two infiltrations of PRP did not reveal any difference between the two groups at short to mid term. A second closely-timed infiltration of PRP to treat proximal patellar tendinopathies is not necessary to improve the efficacy of this treatment in the short term.

1. Introduction

Platelet-rich plasma (PRP), a relatively new treatment for chronic tendinopathies, is obtained by the centrifugation of autologous blood to provide high concentrations of platelets.[1] During degranulation, platelets release various cytokines and growth factors[2] which stimulates differenciation of cells from circulation, improves MMPs-3 expression leading to the remodeling of extra-cell matrix, improves initial stages of healing, as well as neovascularisation and type 1 collagen fiber synthesis and organisation, and gives better maturation of the tendinous cal.[3–5] However, subsequent application of mechanical loads seems to be required for inducing optimal tissue adaptation.[6,7] Despite in vitro and animal experiments having demonstrated this tendon healing process, clinical series are subject to controversy.[8] Studies are difficult to compare, using different PRP preparation methods yielding varying qualities,[9] various injection methods, and different post-infiltration protocols.[8] Even among systematic reviews about the same randomized controlled trials studying PRP treatment for treating lateral epicondylitis, conclusions remain frequently opposite.[10,11] A recent meta-analysis of 13 controlled studies, comprising different tendons (epicondylitis, rotator cuff, patellar and Achilles tendinopathies), showed that PRP injections improved pain at mid-term (3 months) and longer-term (>1 year) compared with control groups.[12] However, these findings cannot be applied to the management of individual patients due to low power and precision demonstrated by this meta-analysis.

Various series studied the effect of PRP in the treatment of patellar tendinopathy, generally with satisfactory results allowing patients to return to sport.[13–15] The most promising results were observed if patients carried out an eccentric rehabilitation protocol.[16] Interestingly, one study demonstrated that PRP leads to a better clinical improvement than ESWT after 1 year.[17] Although it is possible that a single infiltration is efficient in this indication,[15,18] most studies have, surprisingly, evaluated the effects of multiple ($n = 2$ or 3) successive infiltrations.[13,14,17]

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However, the multiplication of infiltrations can reasonably be expected to increase the risks of complications (i.e. infection, pain, neuroalgodystrophy, osteolysis of the patellar pole, etc.),[19–21] and moreover, this treatment can be expensive. For these reasons it seems relevant to evaluate the relative efficacy of two infiltrations of PRP to that of a single treatment.

2. Materials and methods

We used an experimental protocol outlined in our first study.[15] All experimental procedures used in this investigation were approved by the Ethics Committee of the University of Liège (Belgium) (Belgian number B7072018785).

A power calculation showed that with a sample size of 10 subjects in each group, on the VAS scale (taken as the primary endpoint) could be evidenced with a power of 80% at the 5% critical level and a standard deviation of 2.5 if such a difference exists.

Twenty patients (all men), with chronic (more than 3 months) proximal patellar tendinopathy, diagnosed clinically and confirmed by ultrasounds (US) and/or magnetic resonance imaging (MRI), without bone conflict or bone edema, were enrolled. One criteria for inclusion was to have experienced other classical conservative treatments (painkillers, NSAIDs, physiotherapy including eccentric rehabilitation (for more than 20 sessions, 3 times a week, progressively intensified) and shock wave therapy (6 to 9 sessions, 2000 shocks, 9 Hz, 3–4 bars)) which remained unresponsive. Due to pain, their sports capacities were decreased in all cases (Blazina classification >3). They were completely randomized into two groups (one or two infiltrations of PRP, respectively), having first signed an informed consent form.

The assessments were made using a variety of scores:

- 10-Point Visual Analog Scale (VAS);
- Clinical examination using a pressure Algometer Commander (JTech Medical Industries, Salt Lake City, Utah);
- International Knee Documentation Committee form (IKDC);
- Victorian Institute of Sport Assessment—Patellar questionnaire (VISA-P);
- Isokinetic assessment was performed using a Cybex Norm (Cybex International, Medway, Massachusetts, USA) after a 10-min warm-up on a cycle ergometer. The studied modalities were concentric $60^\circ\,s^{-1}$ (C60) and $240^\circ\,s^{-1}$ (C240), and eccentric $30^\circ\,s^{-1}$ (E30) on both quadriceps. A VAS score was used to quantify pain resulting from each test;
- Two days after the isokinetic evaluation, one leg counter movement jump (CMJ) and drop jump (DJ) evaluations were performed using an Optojump device (Microgate, Bolzano-Bozen, Italy), after a 10-min warm-up on a cycle ergometer. A VAS score was also used to quantify pain during each test;
- US (X2000, Siemens, Munich, Germany).

The whole evaluation was made before the infiltration of PRP, and then repeated at an interval of 6 weeks and 3 months after the injection by the same examiner.

As performed in our previous study,[18] 1 year after infiltration, patients were contacted by phone by the same examiner to fill out a standardized questionnaire on the pain severity and the return to sports activities:

- Pain during daily, professional and sports activities;
- The type of sport they practiced (the same or not as before tendinopathy);
- The level of sport they practiced (the same or not as before tendinopathy).

Before platelets were collected, a hematological cell count for each patient was performed under laboratory conditions. PRP was obtained using an apheresis machine (COM.TEC and kit CS5L, Fresenius-Kabi, Bad-Homburg, Germany). We decided to collect platelets with a concentration of around $8.5–9.10^5$ platelets/μL.[22] Samples of the patients' PRP were sent for laboratory analysis for quality control purpose.

Immediately prior to infiltration, 300 μL of $CaCl_2$ were added to the PRP to activate the platelets.[22] Six milliliters of PRP were injected into the patellar tendon after disinfection and US tracking. No local anesthetic was used in order to avoid a decrease in platelet activity linked to a pH modification.[23] Patients were given local cryotherapy immediately following the infiltration. In case of pain, they could not take any anti-inflammatory drugs, but only type I or II classical painkillers.

After 5 to 7 days of relative rest, patients commenced a standardized progressive sub-maximal eccentric program, consisting of 5 sessions of 15 repetitions 3 times a week and supervised by a physical therapist.[16] This eccentric exercise was carried out using the weight of the patient's body, with the back against the wall. The patient would slowly slide his back down the wall until his pathologic leg bent to a 60° angle before pushing on both legs to return to the starting position. A thirty second rest period was allowed between sessions. The patient was treated withed also from electro-stimulation, stretching of the quadriceps, and cryotherapy.

After one week of rehabilitation, a second infiltration of 6 mL of PRP was administered to the 10 subjects of Group 2, following the same protocol. Five to 7 days after the second infiltration, the sub-maximal eccentric protocol was again commenced for another 5 week period (supervised by a physiotherapist). The angulation and the number of sessions were both progressively increased during the rehabilitation, from 60° to 90° and from 5 to 7 sessions of 15 to 20 repetitions, respectively. Ten minutes of cycloergometer exercise, using low resistance, was also added to the program 2 weeks after the second treatment, and proprioception exercises were introduced after 1 month. No sport activities were authorized before 6 weeks. After this period, a progressive and sport-specific training was restarted under medical supervision with the aim of returning completely to sport after 3 months.

Results were expressed as the mean ± standard deviation of the mean (SD). At time 0, the two groups were compared using a Student *t*-test for independent samples, or a Kruskal–Wallis test. Evolution over time for both groups was studied using generalized linear mixed models (GLMM). Differences observed between time 0 and the final evaluation time (12 or 14 weeks for groups 1 and 2, respectively) ((valueTend-valueT0)/(Tend-T0)) were compared between the two groups using a Student *t*-test for independent samples, or a Kruskal-Wallis test. Results were considered significant at the level of uncertainty of 5% ($p < 0.05$). Statistical analyses were conducted using Statistical Analysis System version 9.3 software (SAS Institute, Cary, North Carolina), and graphics of individual developments and averages were created in S-Plus version 8.1 (Tibco Software, Paolo Alto, California).

3. Results

Before the first infiltration, all parameters were homogenous between the groups of 10 subjects, with the exception of VAS ($p = 0.02$), which was worse for Group 1, and IKDC ($p = 0.007$) which was worse for Group 2; these variations do not have any impact on the interpretation of our results. Patient age and duration of symptoms were similar for both groups ($p = 0.68$): 31.1 ± 10.4 y.o. and 17.2 ± 7.4 months in the group 1 and 29.5 ± 5.87 y.o. and 16.9 ± 8.1 months in the group 2. No significant difference in injected PRP