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Intra-articular platelet-rich plasma vs corticosteroids in the treatment of moderate knee osteoarthritis: a single-center prospective randomized controlled study with a 1-year follow up

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Abstract

Background: Osteoarthritis is the most prevalent type of arthritis, which significantly impacts the patient's mobility and quality of life. Pharmacological treatments for osteoarthritis, such as corticosteroids, produce an immediate reduction of the patient's pain as well as an improvement in the patient's mobility and quality of life, but with a limited long-term efficacy. In this context, platelet-rich plasma (PRP) infiltrations represent a therapeutic tool due to its trophic properties and its ability to control inflammatory processes, especially in musculoskeletal applications. The aim of this study is to evaluate and compare the clinical benefits of PRP when injected intra-articularly vs a commonly used corticosteroid (CS, triamcinolone acetonide, Kenalog®) in patients affected by mild to moderate symptomatic knee osteoarthritis.

Methods: Forty patients affected by symptomatic radiologically confirmed knee osteoarthritis (Kellgren-Lawrence grades II–III) were enrolled in this randomized study. Patients randomized in the PRP group (n = 20) received an intra-articular injection of PRP (8 mL) while patients randomized in the CS group (n = 20) received an intra-articular injection of triamcinolone acetonide (1 mL of 40 mg/mL) plus lidocaine (5 mL of 2%). The pain and function of the target knee were evaluated by the VAS, IKDC, and KSS scales at the baseline (V1), 1 week (V2), 5 weeks (V3), 15 weeks (V4), 30 weeks (V5), and 1 year (V6) after treatment.

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Study design, randomization, and intervention

This was a single-center prospective randomized controlled study. Potentially eligible patients with knee pain were pre-screened. Patients, who signed an informed consent and met the inclusion criteria, were considered eligible and assigned in a 1:1 ratio into two groups. The patients were randomized using a computer-generated randomized list. Patients assigned to group one (platelet-rich plasma (PRP)) received one intra-articular injection of autologous PRP. Patients assigned to group two (corticosteroid (CS)) received one intra-articular injection of corticosteroid. The variation from the pain baseline, measured by the VAS score at 1 year (V1), was considered the primary outcome. The VAS pain score was self-completed by the patient. The patient was asked to place a line, perpendicular to the VAS line from the questionnaire, at the point that showed their pain intensity score in their last 7 days of daily activities (walking, working, home activities, house cleaning, and others). Secondary outcomes were the variations in VAS scores, the International Knee Documentation Committee (IKDC 2000 form) score, and the Knee Society Score (KSS) [20] at any time point of the study. All procedures performed in the studies involving human participants were approved by the Latvian local ethics committee and the national health regulatory authority of Latvia. All procedures performed in studies involving human participants were in accordance with the ethical standards of Ethics Committee for Medical and Biomedical Research, Rigas Stradins University (RSU) Ethics Committee, Ref E-9(2), and Riga Eastern Clinical University Hospital Support Foundation. This study was registered at ISRCTN (International Standard Randomized Controlled Trial Number) with the ID ISRCTN46024618, and it was carried out in accordance with the 1964 Declaration of Helsinki. All the patients were informed, before participating in the CT, of the risks of both treatments (including the beneficial and potential adverse effects). Informed consent was obtained from all individual participants included in the study.

PRP preparation method

PRP was prepared using the Hy-Tissue PRP® system, a CE-marked medical device (Fidia, Abano Terme, Italy). To prepare PRP, 18 mL of peripheral blood was collected and 2 mL of 3.8% sodium citrate was added. In order to separate blood components according to their different specific densities, 20 mL of citrated blood was centrifuged at 1800 rpm for 8 min using a Duografter® II centrifuge (Fidia, Abano Terme, Italy). From this resulting plasmatic fraction, 8 mL of pure PRP solution was obtained and used for the intra-articular PRP injection.

Infiltration

Patients in the first group received 8 mL of an intra-articular infiltration of PRP, and patients in the second group received an intra-articular infiltration of 1 mL of 40 mg/mL triamcinolone acetonide (Kenalog®) and 5 mL of 2% lidocaine mixed in a single syringe. Arthrocentesis was permitted in both study groups. All the baseline and follow-up visits were performed by an evaluator who was blinded to the treatment throughout the study. The intra-articular knee injection was performed under sterile conditions, without any local or general anesthesia, with a 20-G × 2.75 70 mm needle using an anterolateral approach. Echographic control (Philips Affinity 70) allowed the correct needle positioning by direct visualization of the PRP/CS liquid injected. After this manipulation, an aseptic cool bandage was applied, for 15 min, for local compression. Non-steroidal anti-inflammatory drugs were prohibited for 10 days following the injection. During the follow-up period, patients carried on their ordinary lives without any specific treatments or restrictions.

Statistical analysis

The sample size calculation used the hypothesis of superiority. The pain was assessed on a visual analog scale (VAS; range 0–10 points) 12 months after the procedure. An average score of 7.3 was assumed in the control group with a standard deviation of 1.6. This meant that detecting a reduction of 1.5 points in the treatment group vs the control group with a power of 80% and 2-sided significance level of 0.05 would require the inclusion of a total of 36 patients. Considering a possible dropout rate of 10%, 40 patients in total were required (20 patients per group). A difference in the VAS of 1.5 points for the average score and a standard deviation between the 2 groups was fixed (based on published results) [16]. The primary and secondary variables were analyzed using the intention-to-treat principle. Categorical variables were described by percentages and frequencies while continuous variables were described by means, standard deviations, and the 95% confidence interval of the mean. Parametric tests (unpaired t test) were used for normal distributions and the Mann-Whitney U test for non-parametric distributions. Data symmetry was analyzed using a D'Agostino and Pearson normality test. Categorical variables were compared using chi-square tests. For all tests, $p < 0.05$ was considered statistically significant. Patient randomization was performed using the "Randomizer for Clinical Trial" software. All statistical analyses were performed using GraphPad Prism version 7.00 for Windows (GraphPad Software, La Jolla, CA, USA).

Table 1 Baseline characteristics of intent-to-treat patients included in the clinical trial

	PRP group ($N = 20$)	Corticosteroid group ($n = 20$)	p value
Gender, M:F, *n*	17:3	15:5	ns
Age, years, mean/SD	66.4 ± 8.4	70.2 ± 9.2	ns
BMI, mean/SD	28.6 ± 5.0	30.5 ± 5.8	ns
K-L degree (II/III), *n*	5:15	6:14	ns
Knee (right/left), *n* (%)	14/6 (70%/30%)	12/8 (60%/40%)	ns
VAS baseline, mean/SD	6.1 ± 1.2	6.0 ± 1.4	ns
KSS baseline, mean/SD	58.3 ± 7.2	54.0 ± 8.2	ns
IKDC baseline, mean/SD	36.6 ± 10.4	30.0 ± 8.8	0.0377

Data are provided as mean ± SD (range), unless indicated otherwise
BMI body mass index, *K-L* Kellgren-Lawrence classification radiographically confirmed, *VAS* visual analog scale, *KSS* Knee Society Score, *IKDC* International Knee Documentation Committee, *ns* not significant

(primary clinical outcome) showed a higher mean change from baseline in the PRP group than the CS group (PRP − 3.1 ± 2.0, − 52%; CS − 0.8 ± 1.8, − 14%). This difference was significant between groups (p = 0.0002). The most surprising effect observed was that PRP induced pain relief just as fast as CS. In fact, a significant reduction of pain from baseline for both groups was found 1 week after treatment (mean VAS change—PRP − 2.8 ± 2.3, − 47%; CS − 3.4 ± 1.2%, − 58%; $p <$ 0.0001). Similarly, significant function improvements from baseline were obtained in the first week for both treatment groups (mean IKDC change—PRP 22.1 ± 16.9, 60%; CS 35.4 ± 10.0, 117%—and mean KSS change—PRP 22.7 ± 12.3, 39%; CS 29.4 ± 12.8, 55%). Interestingly, the pain reduction and the knee functional improvement were not significant between both groups in the very short-term follow-up visit (up to 5 weeks; Table 2). The highest change in the VAS score from the baseline was at 3 months for the PRP group (mean − 4.6 ± 1.6; − 77%) and at 1 month in the CS group (− 3.4 ± 1.2; − 58%).

The pharmacological effect of CS seemed to disappear 15 weeks after receiving treatment as all scores tended to worsen after this period. For instance, pain in the CS group improved rapidly but, in general, worsened after 15 weeks of treatment, and the pain steadily increased in each follow-up visit. At the same time, the PRP group resulted in a sustained improvement in pain relief up to 30 weeks, showing a small increase in pain in the 1-year evaluation follow-up (Fig. 2a). For all other outcome scores, there were significant differences between pre-treatment and post-treatment results at any time, evaluated up to 58 weeks of the follow-up ($p < 0.05$), except for the VAS ($p = 0.1537$) and KSS ($p = 0.1719$) indexes for the CS group at 58 weeks (due to worsening of the pain conditions of the patients).

Knee function improvement was observed in both groups up to 5–15 weeks with no significant differences between groups ($p > 0.05$) (Table 2). At V4 (15 weeks), the PRP group presented a better significant improvement in the IKDC and KSS scores compared to the CS group, which decreased in effectiveness up to 1 year (Fig. 2b, c). Maximum functional improvement and better patient expectation, satisfaction, and activity levels were observed after 15 weeks for the PRP group (mean change from baseline of 41.1 ± 13.6, 112% and 30.2 ± 11.7, 51% for IKDC) and after 5 weeks for the CS group (mean change from baseline of 33.7 ± 13.5, 111% and 29.4 ± 12.8, 55% for KSS).

Safety

No serious adverse events (SAE) occurred. No adverse events were registered in the CS group. Mild synovitis was registered by 15 patients (75%) in the PRP group at the first week after treatment (diagnosed by ultrasound and clinical evaluation: patellar tap test, brush test, fluid displacement, and wave test) that resolved spontaneously. No synovitis was reported from the patients of the CS group.

Discussion

This single-center prospective randomized controlled study showed that a single intra-articular injection of PRP was more efficient than CS for treating moderate OA (Kellgren-Lawrence grades II–III) compared to triamcinolone acetonide. The effectiveness of PRP has been questioned by some authors because the evidence of its efficacy has been highly variable depending on the specific indication [21–24]. Other studies have shown that PRP has been effective for knee OA when compared to placebo, ozone, or HA in several high-quality, randomized, controlled trials [25–29]. Some of these studies suggested that intra-articular infiltrations of PRP provide quantifiable benefits for pain relief and functional improvement within a limited time period (up to 1 year) [25, 28, 29]. For instance, Filardo et al. [30] performed three consecutive intra-articular infiltrations of PRP in a group of 91 patients with chronic degenerative knee

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