Effectiveness of intra-articular injection of platelet-rich plasma in isolated patellofemoral arthritis

Ihab I. El-Desouky

Department of Orthopedics, Faculty of Medicine, Kasr Alainy School of Medicine, Cairo University, Cairo, Egypt

Correspondence to Ihab I. El-Desouky, MD, Department of Orthopedics, Faculty of Medicine, Kasr Alainy School of Medicine, Cairo University, Cairo 11562, Egypt
Tel: +20 237 622 056;
e-mail: ehabede@hotmail.com

Received: 04 March 2022
Revised: 27 March 2022
Accepted: 31 March 2022
Published: 23 September 2022

The Egyptian Orthopaedic Journal 2022, 57:152–6

Background
Adults commonly develop isolated patellofemoral arthritis (PFA). Platelet-rich plasma (PRP) was beneficial in the conservative treatment of tibiofemoral knee osteoarthritis. This study compares patient complaints prior to and following PRP injection for isolated PFA during conservative treatment.
Patients and methods
The study included 18 female patients with unilateral PFA between the ages of 25 and 40. They received a single dose of PRP injections after failing to respond to conservative treatment. The outcome measures, which included the visual analog scale and Kujala scores, were compared with a matched group of 18 patients managed conservatively but successfully. Both groups got the same physiotherapy treatment and kept up with it, until the final assessment for a year.
Results
At the final follow-up, the PRP group's visual analog scale was significantly improved compared with their pre-injection status, with a *P* value of 0.001. However, no statistically significant difference was evident between the PRP and the non-PRP groups that improved with conservative treatment (*P*>0.9). Comparable results were present between the two groups' Kujala scores.
Conclusion
Patients with isolated PFA who do not respond to conservative treatment may benefit from a single PRP injection, which may postpone or eliminate the need for surgical treatment.
Level of evidence: III, a retrospective case–control study.

Keywords:
knee, osteoarthritis, patellofemoral arthritis, platelet-rich plasma

Egypt Orthop J 2022, 57:152–6

1110-1148

Introduction

Isolated patellofemoral osteoarthritis (OA) [patellofemoral arthritis (PFA)] in the absence of coexisting femorotibial pathology is a relatively common condition affecting younger and more active patients, with a prevalence of 5–8% in the general population [1]. The primary symptoms are frequently anterior knee pain (AKP) and crepitus, exacerbated by ascending or descending stairs and rising from or lowering to a sitting position [2]. According to a review of 31 516 knee arthroscopies, 4% of all knees had grade-IV OA. Among these patients, 21% had osteoarthritic lesions on the patella [3]. Its prevalence has increased by 9% in patients over 40, by more than 13% in females, and 15% in males over 60. [1] The lateral facet was the most commonly affected in 89% of cases [4].

Despite its prevalence, treating this painful disorder is difficult due to various possible causes and a lack of knowledge about articular regeneration. The valgus knee alignment accelerates the development of lateral PFA, together with dysplasia of the patella or trochlea and tibial malrotation. The resultant altered direction and strength of the quadriceps femoris contribute to the disease progression [5]. Conservative therapy is the first possibility in isolated PFA treatment due to the complexity of the patellofemoral joint structure and insufficient recognition of the joint's biomechanics. Rest, activity modification, NSAIDs, patellar braces, foot orthoses, patellar banding, exercise, and 'biofeedback' and intra-articular steroid injections are the most influential conservative treatment methods [6]. While a sizable proportion of patients may benefit from conservative methods, some will resist these treatments and eventually require surgery [7].

Recently, biological intra-articular injections such as platelet-rich plasma (PRP) with a higher concentration of platelets have been studied to treat knee OA [8]. The release of growth factors and other molecules, such as platelet-derived growth factor, transforming growth factor-B, type-I insulin-like growth factor-1, and vascular endothelial growth factor, is linked to the efficacy of this treatment [9]. Numerous clinical trials have proved that PRP may be a promising treatment option for OA [10,11]. McLarnon and Heron [12] did a meta-analysis and found that PRP injections were better than steroids at treating OA symptoms.

Although there are few studies on the use of PRP in PFA treatment, promising results are already available [13–16]. As a result, based on the success of treating tibiofemoral knee OA, more research is needed to confirm or disprove these findings. This study aims to compare the results of PRP injections in isolated PFA to a control group that received conservative treatment without PRP injections.

Patients and methods

Patients' enrollment

The participants in the study were 18 females between the ages of 25 and 40 who had isolated unilateral PFA for more than 3 months and had failed conservative treatment. The inclusion criteria were the age range, unilateral PFA, previous failed conservative and physiotherapy program for 6 weeks using visual analog scale (VAS) and Kujala scoring, no obvious lower-extremity deformities, no neurological problems, and no prior knee surgery in the examined limb. The criteria for exclusion included BMI more than 35 kg/m^2, systemic inflammatory diseases, active or chronic infection or history in the knee area, previous knee operation, corticosteroid or hyaluronic acid injection within the previous 12 weeks, bleeding tendency, use of anticoagulant and antiplatelet medications 10 days before injection, use of NSAIDs 2 days before injection, pregnancy, needle phobia, and a platelet count less than 150 000/l. This study was approved by the Institutional Committee Board, Orthopedic Department, Faculty of Medicine, Cairo University. After being fully informed of the benefits and possible adverse effects, written informed consent was obtained from all the patients before the study.

All patients provided written consent after being fully informed of the benefits and possible adverse effects. Prior to PRP treatment, the VAS and Kujala scoring systems assessed clinical data at month 0. The Kujala scoring system assessed subjective symptoms and functional limitations in patellofemoral disorders, including 13 questions. These questions assess knee pain associated with ascending and descending stairs, squatting, running, jumping, and sitting for prolonged flexion, limping, swelling, or patella subluxation, the extent of quadriceps muscle atrophy, flexion deficits, and the need for a walking aid. The scoring system ranges from 0 to 100 points for the best to the worst. Excellent results have a score of 95–100, good results as 84–94, fair results as 65–83, and poor results as 64 [17]. The Arabic version of this scoring system was the tool [18].

An age-matched and BMI-matched group of 18 female patients existed as a control group. These patients received the same conservative treatment as the previous group, but did not receive PRP injections. The regimen began with a 3-week course of anti-inflammatory medications and continued with a 6-week course of physiotherapy and a 12-week home-based program. Patients who achieved a Kujala score of 85 points were excluded from the PRP injection. Radiographic evaluation included (a) anteroposterior weight-bearing radiographs of both knees and (b) lateral (20° of flexion), as well as (c) bilateral tangential patella radiographs (30° of knee flexion). After that, interpretation of all radiographs of both groups was established for patellar affection. Other than that, anteroposterior knee radiographs were looked at for signs of tibiofemoral OA, and they were graded by Kellgren and Lawrence [19].

Preparation and injection of platelet-rich plasma

The GPS III Platelet Concentration System (Biomet Biologics, Warsaw, Indiana, USA) prepared PRP. According to the system's instructions, a sample of patients' venous blood (54 ml) was mixed with 6.0 ml of citrate. The solution was centrifuged at 3200 rpm for 15 min, yielding a 6.0-ml buffy coat layer of leukocyte-rich PRP solution for intra-articular injection. The solution was slowly injected from the lateral aspect of the knee next to the patella while it was mildly subluxated, and the knee was flexed under aseptic conditions with fluoroscopic guidance. After the injection, patients were prescribed knee range-of-motion exercises in the flexion-extension direction. All patients were told to avoid activities that could cause pain for the first 2 days after the injection and rest their knees. NSAIDs were prohibited, but paracetamol and cold compresses were allowed.

Post-injection program

The exercise program began 2 days after the injection with range-of-motion exercises, stretching exercises, and isotonic strengthening exercises for 12 weeks. All the exercises were completed with both legs.

Outcome assessment

The Kujala patellofemoral scoring system was used to evaluate knee function. Patients were evaluated at the start, 6 months later, and 1 year later. Patients

Table 1 Demographic distribution between groups

Variables	PRP group (*N*=18/female)	Non-PRP group (*N*=18/female)	*P* value
Agent	33±5.5	34.7±6.2	0.59
Affected knee (right/left)	10/8	9/9	0.61
Weight (kg)	74.5±9	75.2±8	0.645
Height (cm)	165.7±10	167.4±9	0.216
BMI (kg/m^2)	27.1±7	26.8±8	0.745

PRP, platelet-rich plasma.

Table 2 Visual analog scale and Kujala score

Final follow-up	Pre-injection	Post injection	*P* value (pregroup and postgroup)	Non-PRP	*P* value (post-PRP and non-PRP groups)
VAS (mean±SD)	5±1	1.5±1.2	<0.001	1.5±1	0.72
Kujala (mean±SD)	72±4.8	89.8±2.4	< 0.001	89.6±3	0.36

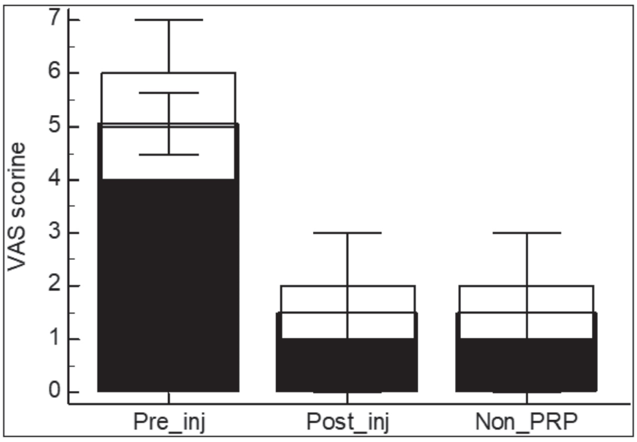
PRP, platelet-rich plasma; VAS, visual analog scale.

were questioned about the side effects during each round. All the patients' parameters were recorded on the same follow-up form. The patient's subjective self-assessment of pain was scored on a VAS between 0 and 10 points (0=no pain, 10=severe pain).

Statistical analysis

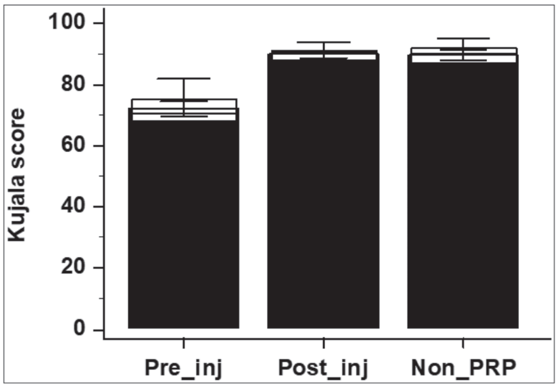
The data were analyzed using SPSS (Statistical Package for Social Science) 15.0 for Windows (Chicago, Illinois, USA). For continuous variables, descriptive statistics were defined as mean/SD or minimum to maximum, while for nominal variables, they were defined as case number and percentage. The Student *t* test was used to compare the spread of continuous variables to the normal spread. The χ^2 test was used to compare discrete variables.

Figure 1



VAS score for pre-PRP-injection status, post-PRP-injection, and non-PRP-injection group. PRP, platelet-rich plasma; VAS, visual analog scale.

Figure 2



Kujala score for pre-PRP-injection status, post-PRP-injection, and non-PRP-injection group. PRP, platelet-rich plasma.

Results

There was no statistically significant difference in demographic data properties between the groups (Table 1).

The VAS was significantly improved in the PRP group at the final follow-up compared with the pre-injection status, with a *P* value less than 0.001. However, when compared with the non-PRP group that improved with conservative treatment (P>0.9), no significant difference was observed. The summary of the outcomes is shown in Table 2. Comparable results were obtained when the Kujala score was compared in three different situations (Figs 1 and 2).

No complications, local or general, were observed during or following injections.

Discussion

In this study, patients who did not respond to conservative treatment achieved favorable outcomes following PRP injection and physiotherapy. The findings showed the efficacy of PRP injection as a nonoperative treatment option for resistant isolated PFA. AKP is the most common reason adolescents, adults, and physically active individuals consult with a knee orthopedic surgeon [20]. AKP was thought to be caused by chondromalacia patellae until the late 1960s. Numerous authors, however, have been unable to link AKP and chondromalacia patellae conclusively [21]. In the 1970s, AKP was frequently associated with patellofemoral malalignment, and frequently treated surgically, with mixed results [22]. The tissue homeostasis theory was proposed in the 1990s by Scott F. Dye and his research group at the University of California, San Francisco. According to this theory, joints are not merely mechanical structures; they are living, metabolically active systems. Pain is caused by a mosaic of physiopathological factors, including increased osseous remodeling, increased intraosseous pressure, and peripatellar synovitis, resulting in a reduced 'envelope of function' and pain [23,24]. According to Dye's envelope of load-acceptance theory, overuse or cyclical overload of soft tissue or bone areas may account for AKP in many patients who do not have patellofemoral or limb malalignment. Hyperinnervation of the patellar lateral retinacula results in decreased susceptibility to stress and pain [25]. Additionally, stress cycles induce periodic ischemic states in the patellar cartilage. Selfe *et al*. [26] classified AKP patients into three groups based on their oxygenation status: hypoxic, inflammatory, or mechanical. On the other hand, ischemia may be the source of pain in all three groups, as inflammatory changes can occur following stress-induced cartilage ischemia and mechanical damage to the vascular system.

These theories can be summarized as follows: abnormal PF joint alignment and trochlear morphology (patella alta and patellar tilt), kinetic and kinematic abnormalities (quadriceps muscle size, strength, and force), rupture and reconstruction of the anterior cruciate ligament, female sex, age, and BMI have all been identified as risk factors for progression of PF cartilage deterioration by affecting the functional envelope [27]. Strengthening and gait retraining is currently the primary stay of treatment for PFA. Additionally, in mild-to-moderate cases, nonoperative measures such as cortisone injections, hyaluronic acid injections, orthobiologics such as PRP or stem cell injections, and passive patellar maltracking correction using bracing and taping may be beneficial. Conservative measures are ineffective after 3–6 months, showing the need for surgical intervention [28].

PRP contains high concentrations of growth factors that regulate chondral homeostasis and benefit both the healing and chondrogenesis processes. In vitro, PRP stimulates the cellular proliferation and matrix synthesis of chondrocytes. By supplementing the culture medium with PRP, porcine chondrocytes, collagen, and proteoglycan syntheses are increased [29]. PRP demonstrated a beneficial effect on cartilage repair and restoration following microfractures in animal and human studies [30,31]. Moussa *et al.* [32] demonstrated that PRP has a beneficial effect on chondrocytes, synovial, and stem mesenchymal cells by increasing cell proliferation, extracellular matrix production, and hyaluronic acid syntheses. PRP can also act as a bioactive scaffold in cartilage defects.

Numerous meta-analyses of randomized trials have supported the efficacy of PRP intra-articular knee injection in treating tibiofemoral OA [11,12,33–38]. However, treating PFA with intra-articular injections has been linked to a worse outcome [39]. On the other hand, some studies yielded positive results [13–16].

The GPS III Platelet Concentration System was used to prepare the PRP, and injection was performed using the buffy coat layer. The composition of this layer was analyzed and found to contain increased platelet concentrations (three to six times that of the patient's baseline), as well as increased white blood cell concentrations (three to six times that of the patient's baseline); these included neutrophils, leukocytes, and monocytes, and was dubbed leukocyte-rich-PRP. White blood cells may modulate inflammatory and platelet activation, thereby enhancing the tissue repair mechanism [40]. Zimmermann *et al.* [41] discovered that an increase in white blood cell count explained between one-third and half of the variation in growth factors observed in their samples. They discovered a positive correlation between the white blood cell count and vascular endothelial growth factor levels (a protein known to be produced by white blood cells) and platelet-derived growth factor. Patients with isolated PRP who do not respond to initial conservative management may benefit from a single well-prepared PRP injection that lasts at least 1 year. This management mode may benefit this patient population and result in a delay or cessation of surgical treatment. We found no adverse events associated with the use of PRP injections. Rai *et al*. [42] reported that nine (9.18%) of their patients experienced headaches, dizziness, sweating, and syncope for ~20–30 min following intra-articular PRP injection. Patel hypothesized that the adverse effects of PRP were caused by the higher $CaCl_2$ concentration used to prepare the sample [43]. The study's limitations include a small sample size, an observational design with no intention of randomization, and a brief follow-up period. We recommend additional research to address all of these limitations. However, the study has some strong points, such as the presence of a control group and the strict selection of patients to allow for a more thorough analysis of the outcomes.

Conclusion

The findings support PRP injections to treat patients with isolated PFA resistant to conservative management.

Acknowledgements

Authors' contribution: I.E.E. wrote the main manuscript text and prepared figures, tables, and statistics. I.E.E. also reviewed the paper.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Davies AP, Vince AS, Shepstone L, Donell ST, Glasgow MM. The radiologic prevalence of patellofemoral osteoarthritis. Clin Orthop Relat Res 2002; 402:206–212.
2 Schiphof D, Van Middelkoop M, De Klerk BM, Oei EH, Hofman A, Koes BW, *et al*. Crepitus is a first indication of patellofemoral osteoarthritis (and not of tibiofemoral osteoarthritis). Osteoarthritis Cartilage 2014; 22:631–638.
3 Curl WW, Krome J, Gordon ES, Rushing J, Smith BP, Poehling GG. Cartilage injuries: a review of 31,516 knee arthroscopies. Arthroscopy 1997; 13:456–460.
4 Iwano T, Kurosawa H, Tokuyama H, Hoshikawa Y. Roentgenographic and clinical findings of patellofemoral osteoarthrosis. With special reference to its relationship to femorotibial osteoarthrosis and etiologic factors. Clin Orthop Relat Res 1990; 252:190–197.
5 Katchburian MV, Bull AMJ, Shih YF, Heatley FW, Amis AA. Measurement of patellar tracking: assessment and analysis of the literature. Clin Orthop Relat Res 2003; 412:241–259.
6 Crossley KM, Cook JL, Cowan SM, *et al*. Anterior knee pain. In: Brukner PD, Bahr R, Blair S, *et al*. Brukner and Khan's clinical sports medicine. Sydney: McGraw Hill; 2012. 684–714.
7 Kettunen JA, Visuri T, Harilainen A, Sandelin J, Kujala UM. Primary cartilage lesions and outcome among subjects with patellofemoral pain syndrome. Knee Surg Sports Traumatol Arthrosc 2005; 13:131–134.
8 Demange MK, Sisto M, Rodeo S. Future trends for unicompartmental arthritis of the knee: injectables & stem cells. Clin Sports Med 2014; 33:161–174.
9 Zhu Y, Yuan M, Meng HY, Wang AY, Guo QY, Wang Y, *et al*. Basic science and clinical application of platelet-rich plasma for cartilage defects and osteoarthritis: a review. Osteoarthritis Cartilage 2013; 21:1627–1637.
10 Bennell KL, Hunter DJ, Paterson KL. Platelet-rich plasma for the management of hip and knee osteoarthritis. Curr Rheumatol Rep 2017; 19:24.
11 Shen L, Yuan T, Chen S, Xie X, Zhang C. The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials. J Orthop Surg Res 2017; 12:16.
12 McLarnon M, Heron N. Intra-articular platelet-rich plasma injections versus intra-articular corticosteroid injections for symptomatic management of knee osteoarthritis: systematic review and meta-analysis. BMC Musculoskelet Disord 2021; 22:550.
13 Örsçelik A, Yildiz Y. Comparison of single and triple platelet rich plasma injections in the treatment of patellofemoral pain syndrome. Turki Klin J Med Sc 2015; 35:78–87.
14 Örsçelik A, Akpancar S, Seven MM, Erdem Y, Koca K. The efficacy of platelet rich plasma and prolotherapy in chondromalacia patella. Turk J Sports Me 2019; 55:28–37.
15 Pintat J, Silvestre A, Magalon G, Gadeau AP, Pesquer L, Perozziello A, *et al*. Intra-articular injection of mesenchymal stem cells and platelet-rich plasma to treat patellofemoral osteoarthritis: preliminary results of a long-term pilot study. J Vasc Interv Radiol 2017; 28:1708–1713.
16 Cobianchi Bellisari F, De Marino L, Arrigoni F, Mariani S, Bruno F, Palumbo P, *et al*. T2-mapping MRI evaluation of patellofemoral cartilage in patients submitted to intra-articular platelet-rich plasma (PRP) injections. Radiol Med 2021; 126:1085–1094.
17 Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. Arthroscopy 1993; 9:159–163.
18 Hamdan M, Haddad B, Isleem U, Hamad A, Hussein L, Shawareb Y, *et al*. Validation of the Arabic version of the Kujala patellofemoral pain scoring system. J Orthop Sci 2019; 24:290–293.
19 Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis 1957; 16:494–502.
20 Sanchis-Alfonso V, McConnell J, Monllau JC, Fulkerson JP. Diagnosis and treatment of anterior knee pain. J ISAKOS 2016; 1:161–173.
21 Dye SF. The pathophysiology of patellofemoral pain: a tissue homeostasis perspective. Clin Orthop Relat Res 2005; 436:100–110.
22 Insall JN. Patella pain syndromes and chondromalacia patellae. Instr Course Lect 1981; 30:342–356.
23 Dye SF. The knee as a biologic transmission with an envelope of function: a theory. Clin Orthop Relat Res 1996; 325:10–18.
24 Dye SF, Stäubli HU, Biedert RM, Vaupel GL. The mosaic of pathophysiologycausing patellofemoral pain: therapeutic implications. Oper Tech Sports Med 1999; 7:46–54.
25 Sanchis-Alfonso V, Roselló-Sastre E, Monteagudo-Castro C, Esquerdo J. Quantitative analysis of nerve changes in the lateral retinaculum in patients with isolated symptomatic patellofemoral malalignment. A preliminary study. Am J Sports Med 1998; 26:703–709.
26 Selfe J, Kärki A, Stevens D. A review of the role of circulatory deficit in the genesis of patellofemoral pain. Phys Ther Rev 2002; 7:169–172.
27 Peat G, Duncan RC, Wood LRJ, Thomas E, Muller S. Clinical features of symptomatic patellofemoral joint osteoarthritis. Arthritis Res Ther 2012; 14:R63.
28 Dejour D, Allain J. Isolated patellofemoral osteoarthritis: natural history and clinical presentation. In: Zaffagnini S, Dejour D, Arendt EA eds. Patellofemoral pain, instability, and arthritis: clinical presentation, imaging, and treatment. Berlin: Springer Berlin Heidelberg; 2010. 263–70.
29 Akeda K, An HS, Okuma M, Attawia M, Miyamoto K, Thonar EJ, *et al*. Platelet-rich plasma stimulates porcine articular chondrocyte proliferation and matrix biosynthesis. Osteoarthr Cartil 2006; 14:1272–1280.
30 Milano G, Sanna Passino E, Deriu L, Careddu G, Manunta L, Manunta A, *et al*. The effect of platelet rich plasma combined with microfractures on the treatment of chondral defects: an experimental study in a sheep model. Osteoarthr Cartil 2010; 18:971–980.
31 Lee GW, Son JH, Do KJ, Jung GH. Is platelet-rich plasma able to enhance the results of arthroscopic microfracture in early osteoarthritis and cartilage lesion over 40 years of age?. Eur J Orthop Surg Traumatol 2013; 23:581–587.
32 Moussa M, Lajeunesse D, Hilal G, El Atat O, Haykal G, Serhal R, *et al*. Platelet rich plasma (PRP) induces chondroprotection via increasing autophagy, anti-inflammatory markers, and decreasing apoptosis in human osteoarthritic cartilage. Exp Cell Res 2017; 352:146–156.
33 Filardo G, Previtali D, Napoli F, Candrian C, Zaffagnini S, Grassi A. PRP injections for the treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. Cartilage 2021; 13(1_suppl):364S–375S.
34 Gato-Calvo L, Magalhaes J, Ruiz-Romero C, Blanco FJ, Burguera EF. Platelet-rich plasma in osteoarthritis treatment: review of current evidence. Ther Adv Chronic Dis 2019; 10:1–18.
35 Kon E, Di Matteo B, Delgado D, Cole BJ, Dorotei A, Dragoo JL, *et al*. Platelet-rich plasma for the treatment of knee osteoarthritis: an expert opinion and proposal for a novel classification and coding system. Expert Opin Biol Ther 2020; 20:1447–1460.
36 Migliorini F, Driessen A, Quack V, Sippel N, Cooper B, Mansy YE, *et al*. Comparison between intra-articular infiltrations of placebo, steroids, hyaluronic and PRP for knee osteoarthritis: a Bayesian network meta-analysis. Arch Orthop Trauma Surg 2021;141:1473–1490.
37 Dai WL, Zhou AG, Zhang H, Zhang J. Efficacy of platelet-rich plasma in the treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. Arthroscopy 2017; 33:659–670.e1.
38 Meheux CJ, McCulloch PC, Lintner DM, Varner KE, Harris JD. Efficacy of intra-articular platelet-rich plasma injections in knee osteoarthritis: a systematic review. Arthroscopy 2016; 32:495–505.
39 Jang SJ, Kim J Do, Cha SS. Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. Eur J Orthop Surg Traumatol 2013; 23:573–580.
40 Fitzpatrick J, Bulsara MK, McCrory PR, Richardson MD, Zheng MH. Analysis of platelet-rich plasma extraction: variations in platelet and blood components between 4 common commercial kits. Orthop J Sport Med 2017; 5:232596711667527.
41 Zimmermann R, Jakubietz R, Jakubietz M, Strasser E, Schlegel A, Wiltfang J, *et al*. Different preparation methods to obtain platelet components as a source of growth factors for local application. Transfusion 2001; 41:1217–1224.
42 Rai D, Singh J, Somashekharappa T, Singh A. Platelet-rich plasma as an effective biological therapy in early-stage knee osteoarthritis: one year follow up. SICOT-J 2021; 7:6.
43 Patel S, Dhillon MS, Aggarwal S, Marwaha N, Jain A. Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. Am J Sports Med 2013; 41:356–364.