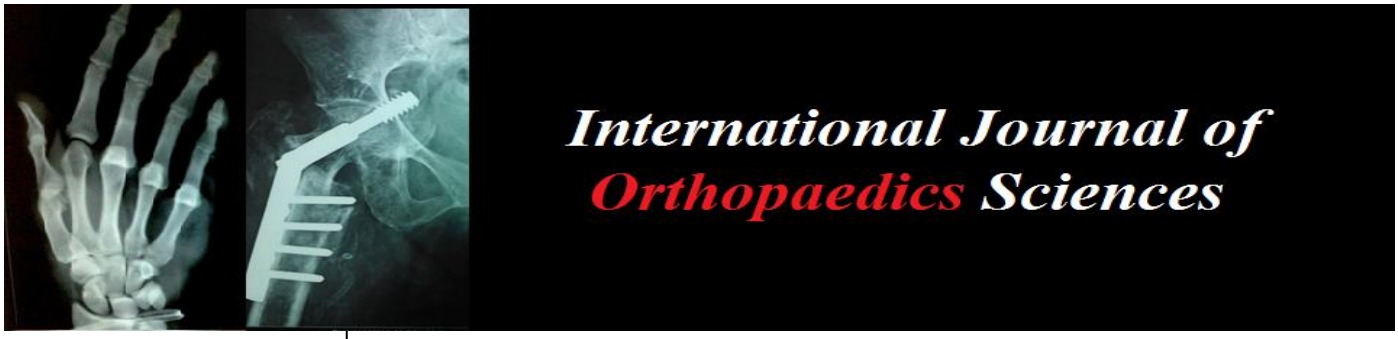

E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2022; 8(1): 811-814

www.orthopaper.com
Received: 21-11-2021
Accepted: 09-01-2022

Dr. NC Arora
Professor, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Dr. Vipul Ahir
Post Graduate Resident, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Dr. Pindaria Kuldeep Prakashchandra
Post Graduate Resident, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Dr. Kartik Dua
Post Graduate Resident, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Dr. Naveen Taxak
Senior Resident, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Dr. Dhamelia Dhyey Shambhubhai
Post Graduate Resident, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Dr. Avinash Kumar Singh
Post Graduate Resident, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Dr. Savsaviya Ram Gordhanbhai
Post Graduate Resident, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

Corresponding Author:
Dr. NC Arora
Professor, Department of Orthopaedics, SGT Medical College, Hospital & Research Institute, Gurugram, Haryana, India

A prospective study to analyse functional outcome of intraarticular autologous platelet rich plasma (PRP) in management of osteoarthritis of knee joint

Dr. NC Arora, Dr. Vipul Ahir, Dr. Pindaria Kuldeep Prakashchandra, Dr. Kartik Dua, Dr. Naveen Taxak, Dr. Dhamelia Dhyey Shambhubhai, Dr. Avinash Kumar Singh and Dr. Savsaviya Ram Gordhanbhai

DOI: https://doi.org/10.22271/ortho.2022.v8.i1k.3105

Abstract
Knee osteoarthritis (OA) is a usual problem in the elderly population, which is treated with lifestyle modifications, non-steroidal anti-inflammatory drugs, physiotherapy, and intraarticular injections of corticosteroids/hyaluronic acid/autologous platelet-rich plasma (PRP) in the early stages, and in the late stages, surgical procedures, such as arthroscopic debridement, unicompartmental arthroplasty, patellofemoral arthroplasty, and total knee replacement, are performed. Gradually, there is an increasing trend in the use of intraarticular autologous PRP for treatment of Kellgren Lawrence grade 1 and 2 knee OA. This prospective study aimed to assess the functional outcome of patients with OA when treated with autologous intraarticular PRP for a follow-up period of up to 15 months.
This study included 40 individuals with Kellgren Lawrence grade 1 and 2 knee OA who were aged 50–70 years and treated with single autologous intraarticular PRP injection and followed at 1, 3, 6, 12, and 15 months after injection, and visual analog scale (VAS) score was calculated at each follow-up.
Preprocedure VAS score of all patients was obtained as 100 mm, and the VAS score was calculated at follow-up on 1, 3, 6, 12, and 15 months and ranged from 13 to 45.

Keywords: Knee osteoarthritis, platelet-rich plasma, intraarticular injection, VAS

Introduction
Knee osteoarthritis (OA) is the most common chronic and degenerative articular disease, a source of pain and the chief cause of disability and dependence among the adult population [1]. The knee is the largest synovial joint in humans [2]. Knee OA is a degenerative disease of the knee joint and typically the result of wear and tear and progressive loss of articular cartilage, resulting in pain, fatigue, functional limitations, increased healthcare utilization, and high economic costs to society [3]. These symptoms significantly restrict the individual's ability to get up from a chair, walk, or climb the stairs. Walking with a limp, poor alignment of the limb, and instabilities can also be observed in individuals with OA [4].
The diagnosis of knee OA is made primarily based on weight-bearing skiagrams of the knee in anteroposterior (AP) and lateral views.

Autologous Platelet-Rich Plasma (PRP)
PRP is defined as "a volume of plasma that has a platelet count above baseline blood platelet count5." To obtain PRP, 50 mL venous blood is drawn from the patient and centrifuged to separate PRP from red blood cells and plasma [6]. This autologous PRP is injected intraarticularly in the affected knee joint. The first studies on PRP preparations were conducted in the 1950s and investigated coagulation [7].
When the platelets degranulate after injection, growth factors, such as transforming growth factor beta, platelet-derived growth factor, epidermal growth factor, vascular endothelial growth factor, fibroblast growth factor, and insulin-like growth factor, are released. These growth factors are believed to have regenerative capacity. More importantly, in OA, they may inhibit inflammatory effects on chondrocytes by nuclear factor kappa-light-chain-enhancer of activated B cells and interleukin 1 [8].

Types of PRP

In 2009, Dohan Ehrenfest *et al.* [9] proposed a classification of four main families of preparations following two principle parameters: presence or absence of a cell content (e.g., leukocytes) and fibrin architecture:

1. Pure PRP or leukocyte-poor PRP: the preparation obtained has no leukocytes and provides a low-density fibrin network after activation.
2. Leukocyte and PRP: preparations contain leukocytes and show a low-density fibrin network after activation.
3. Pure platelet-rich fibrin (PRF) or leukocyte-poor PRF: preparations obtained has no leukocytes and high-density fibrin network. Unlike pure PRP or PRP containing leukocytes, these products cannot be injected and exist in an activated gel form.
4. Leukocyte-rich fibrin and PRF: preparations have leukocytes and high-density fibrin network.

Materials and methods

This prospective study was conducted in the Department of Orthopaedics at Shree Guru Gobind Singh Tricentenary Medical College, Hospital, and Research Institute, Budhera, Gurgaon. After obtaining informed consent from patients, 40 symptomatic patients with Kellgren Lawrence grade [10] 1 and 2 OA who were aged 50 –70 years and had body mass index ≤ 30 were included in the study.

All patients were evaluated on an outpatient basis. A detailed history was obtained, and a physical examination performed. Patients were investigated to rule out other forms of inflammatory arthritis. The patient's complaints were recoded according to the visual analog scale (VAS) scale. VAS scale (Figure 1) was considered to be 100 mm in all patients at the initiation of the study and at follow-up visits at 1, 3, 6, 12, and 15 months. Patients were asked to mark on a point between 0 to 100 mm (0 being no pain and 100 being pain similar to that before the procedure). After the patient has marked a point, it was measured using the VAS. A low VAS score suggests better pain relief, and high VAS score suggests otherwise. Weight-bearing AP and lateral skiagram of the knee were obtained to grade knee OA.

Before the procedure, pain was marked as 100 mm on the VAS in every patient, and in all follow-up visits, patients were requested to spot a point on the scale to determine the degree of pain.

Results Graded As Per VAS Ipgrading

Excellent, > 80% pain relief
Good, 60%–80% pain relief
Fair, 40%–60% pain relief
Poor, <40% pain relief

No non-steroidal anti-inflammatory drugs were administered to the patients during this study interval, except in four patients who received paracetamol 500 mg tablet orally twice a day for 1 day. All patients were advised to rest and apply cold compression for 1 day after the procedure.

Materials

- PRP: It is defined as plasma with higher platelet count compared to baseline blood

Methodology

Particularly, 30–50 mL of venous blood was collected from patients in sterile acid citrate dextrose tubes, which yields approximately 5–8 mL of PRP.

In this PRP method, primary centrifugation is conducted to separate red blood cells (RBCs), which is followed by secondary centrifugation to concentrate platelets that are present in the smallest final plasma volume. The primary spin is performed at 1500 rotation per minute (RPM) for 18 min to distinguish RBC from the remaining whole blood. After primary spin, the whole blood separates into three layers, that is, plasma with suspended platelets, buffycoat, and RBC. For PRP preparation, the upper plasma layer and buffycoat are transferred to empty sterile tubes. The second spin is performed at 2500 RPM for 10 min. The upper layer that contains mostly platelet poor plasma is discarded. Pellets of platelets are concentrated in the bottom one-third of the tube, which consists of PRP.

Platelet count of whole blood and PRP was also compared. The platelet concentration was found to be at least more than fivefold higher in PRP compared to whole blood/baseline blood.

Procedure

Single injection of 6–8 mL of PRP was administered into the knee joint through the superolateral approach using a 21-G needle. Patients were advised to take rest and cold compression for 1 day.

Follow-up of patients was conducted at 1, 3, 6, 12, and 15 months after injection. At each follow-up visit, the knee was examined thoroughly, and the patient was requested to spot the degree of pain on the VAS.

Statistical Analysis

Data were analyzed using repeated analysis of variance. Statistical program was used to perform statistical analysis, and P-values < 0.05 were considered significant.

Results

In our study, there is statistically significant improvement in VAS up to 15 months.

In this study, the mean age of patients was 58 years. Almost all patients had symptomatic pain relief and better joint function. The detailed results are presented in Table 1.

Table 1: Follow-up and results after injection of PRP

Follow-up duration	Number of patients N	VAS range	Mean VAS	Inference
On the day of the procedure	n = 40	100–100 mm	100 mm	-
At 1 month	n = 40	13–33 mm	25 mm	Good improvement
At 3 months	n = 40	12–28 mm	19 mm	Excellent improvement
At 6 months	n = 40	15–31 mm	23 mm	Good improvement
At 12 months	n = 40	19–41 mm	25 mm	Good improvement
At 15 months	n = 40	19–45 mm	27 mm	Good improvement

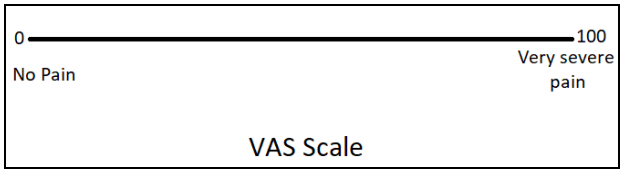

Fig 1: Visual Analog Scale (VAS)

Discussion

Pharmacological treatment, such as NSAID, viscosupplementations, and glucocorticoids have been suggested as noninvasive solutions to manage pain and improve joint mobility, all with variable success rates.

The present-day treatment scheme based on evidence and expert opinion outline the balancing approach with nonpharmacological treatment, pharmacotherapy, and eventually surgical management when all management fails.

The higher pervasiveness and increasing load of knee OA along with current safety concerns regarding pharmacological interventions has surged the requirement for new efficacious modalities to treat OA by repairing damage of the cartilage other than just alleviating the symptoms. While addressing the abovementioned issues, the number of surgical procedures could be decreased significantly.

PRP stimulates tissue regeneration. It also slows the degeneration of the cartilage by movement, multiplication, and differentiation of mesenchymal stem cells into articular chondrocytes [11].

In this study, we used single injection of leukocyte-poor PRP (LP-PRP). Sample for PRP was extracted using double spinning technique with platelet concentration in sample more than five times that of the baseline blood.

A number of studies showed the therapeutic benefit of intraarticular PRP injection in the management of knee OA [12–23].

A meta-analyses study conducted by Pu Chen *et al.* in 2019 on 1677 patients suggested that, for a short-term follow-up (≤ 1 year), intraarticular PRP injection is better in pain relief and functional improvement in patients with OA knee than hyaluronic acid (HA) and placebo. It also concluded that there is no variance in risk and adverse effect occurrence between PRP and HA or placebo [24]. In 2017, Shen *et al.* concluded that there were no severe complications recorded after PRP injection and all adverse reactions were self-resolved in days [23]. One meta-analysis demonstrated that PRP injection showed better analgesia and functional improvement compared to HA in the 12 months follow-up [18]. In 2015, Riboh *et al.* conducted a network meta-analysis to compare the clinical outcomes and adverse effects of PRP compared to LR-PRP, HA, and placebo in the management of knee OA [25]. In 2010, Kon *et al.* conducted a prospective study on 100 patients affected with knee OA and concluded that management of knee OA with PRP is safe and has capability to decrease pain and improve functionality of knee and quality of life [26].

No major complications or other major adverse reaction developed in patients included in the study. Studies from Kon *et al.* [26], Sampson *et al.* [27], and Filardo *et al.* [28] supported the same findings.

In our study, four patients had short-term exacerbation of knee pain after injection. Pain resolved spontaneously in 1 day. Pain is caused by the abrupt increase in volume of intracapsular contents, stretching the knee joint capsule. In 2012, Spakova´ *et al.* [29] and Maheshwari *et al.* [30] in 2017 also recorded abrupt onset of knee pain after PRP injection in 6 of 60 patients and 7 of 58 patients, respectively.

In our study, during the follow-up period, significant improvements were noted in symptoms and VAS scores of a majority of patients compared to their pre-injection values.

Conclusion

Forty patients with early knee OA (grades 1 and 2) were treated with single intraarticular autologous PRP. The patient acceptance for the procedure is good as the material used is autologous and had low cost. Patients were followed for 15 months, and there is excellent response at 1 month, but a good response was maintained up to 15 months.

This procedure is good for use in patients with Kellgren Lawrence grade 1 and 2 knee OA.

References

1. Wang-Saegusa A, Cugat R, Ares O, *et al*. Infiltration of plasma rich in growth factors for osteoarthritis of the knee short-term effects on function and quality of life. Arch Orthop Trauma Surg. 2011;131:311-7.
2. Da Costa BR, Hari R, Jüni P: Intra-articular corticosteroids for osteoarthritis of theKnee. JAMA. 2016;316:2671-72.
3. Litwic A, Edwards MH, Dennison EM, *et al*. Epidemiology and burden of osteoarthritis. Br Med Bull. 2013;105:185-99.
4. Losina E, Weinstein AM, Reichmann WM, *et al*. Lifetime risk and age at diagnosis of symptomatic knee osteoarthritis in the US. Arthritis Care Res (Hoboken). 2013;65:703-11.
5. Marx RE. Platelet-rich plasma (PRP): what is PRP and what is not PRP? Implant Dent. 2001;10:225-28.
6. Howard D, Shepherd JH, Kew SJ, *et al.* Release of growth factors from a reinforced collagen GAG matrix supplemented with platelet rich plasma: influence on cultured human meniscal cells. J Orthop Res. 2014;32:273-8.
7. Kingsley CS. Blood coagulation; evidence of an antagonist to factor VI in platelet-rich human plasma. Nature. 1954;173:723-24.
8. Dhillon RS, Schwarz EM, Maloney MD. Platelet-rich plasma therapy - future or trend? Arthritis Res Ther. 2012;14:219.
9. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol. 2009;27:158-67.
10. Kellgren JH, Lawrence JS: Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957;16:494-502.
11. Sakata R, Reddi AH. Platelet-rich plasma modulates actions on articular cartilage lubrication and regeneration. Tissue Eng Part B Rev. 2016;22:408-19.
12. Di Sante L, Villani C, Santilli V, *et al*. Intra-articular hyaluronic acid vs platelet-rich plasma in the treatment of hip osteoarthritis. Med Ultrason. 2016 Dec 5 ;18:463-8.
13. Vannabouathong C, Del Fabbro G, Sales B, *et al*. Intra-articular injections in the treatment of symptoms from ankle arthritis: A systematic review. Foot Ankle Int. 2018 Oct ;39:1141-50.
14. Görmeli G, Görmeli CA, Ataoglu B, *et al*. Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. Knee Surg Sports Traumatol Arthrosc. 2017;25:958-65.
15. Patel S, Dhillon MS, Aggarwal S, *et al*. Treatment with

platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. Am J Sports Med. 2013 Feb ;41:356-64.
16. Sánchez M, Fiz N, Azofra J, *et al*. A randomized clinical trial evaluating plasma rich in growth factors (PRGF-Endoret) versus hyaluronic acid in the short-term treatment of symptomatic knee osteoarthritis. Arthroscopy. 2012 Aug ;28:1070-8.
17. Filardo G, Di Matteo B, Di Martino A, *et al*. Platelet-rich plasma intra-articular knee injections show no superiority versus viscosupplementation: A randomized controlled trial. Am J Sports Med. 2015 Jul ;43:1575-82.
18. 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 Mar ;33:659-670.e1.
19. Xu Z, Luo J, Huang X, *et al*. Efficacy of platelet-rich plasma in pain and self-report function in knee osteoarthritis: A best-evidence synthesis. Am J Phys Med Rehabil. 2017 Nov ;96:793-800.
20. Kanchanatawan W, Arirachakaran A, Chaijenkij K, *et al*. Short-term outcomes of platelet-rich plasma injection for treatment of osteoarthritis of the knee. Knee Surg Sports Traumatol Arthrosc. 2016 May ;24:1665-77.
21. Shen L, Yuan T, Chen S, *et al*. 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 Jan 23;12:16.
22. Campbell KA, Saltzman BM, Mascarenhas R, *et al*. Does intra-articular platelet-rich plasma injection provide clinically superior outcomes compared with other therapies in the treatment of knee osteoarthritis? A systematic review of overlapping meta-analyses. Arthroscopy. 2015 Nov, 31:2213-21.
23. Sadabad HN, Behzadifar M, Arasteh F, *et al*. Efficacy of Platelet-Rich plasma versus hyaluronic acid for treatment of Knee osteoarthritis: A systematic review and meta-analysis. Electron Phys. 2016 Mar 25;8:2115-22.
24. Chen P, Huang L, Ma Y, *et al*. Intra-articular platelet-rich plasma injection for knee osteoarthritis: a summary of meta-analyses. J Orthop Surg Res. 2019;14:385.
25. Riboh JC, Saltzman BM, Yanke AB, *et al*. ffect of leukocyte concentration on the efficacy of platelet-rich plasma in the treatment of knee osteoarthritis. Am J Sports Med. 2016 Mar ;44:792-800.
26. Kon E, Buda R, Filardo G, *et al*. Platelet-rich plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesions. Knee Surg Sports Traumatol Arthrosc. 2010 Apr ;18:472-9.
27. Sampson S, Reed M, Silvers H, *et al*. Injection of platelet-rich plasma in patients with primary and secondary knee osteoarthritis: a pilot study. Am J Phys Med Rehabil. 2010;89:961-9.
28. Filardo G, Kon E, Pereira Ruiz MT, *et al*. Platelet-rich plasma intra-articular injections for cartilage degeneration and osteoarthritis: single- versus double-spinning approach. Knee Surg Sports Traumatol Arthrosc 2012, 20:2082-91.
29. Spaková T, Rosocha J, Lacko M, *et al*. Treatment of knee joint osteoarthritis with autologous platelet-rich plasma in comparison with hyaluronic acid. Am J Phys Med Rehabil. 2012;91:411-7.
30. Maheshwari P, Harshwardhan H. Platelet rich plasma for the treatment of osteoarthrosis knee. Int J Res Orthop. 2017;3:242-6.