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Dr. Anand Kumar

PG Student, Department of
Orthopaedics, Darbhanga
Medical College and Hospital,
Darbhanga, Bihar, India

Dr. Nand Kumar

Professor and HOD, Department
of Orthopaedics, Darbhanga
Medical College and Hospital,
Darbhanga, Bihar, India

Dr. Ashutosh Kumar

Assistant Professor,
(Orthopaedics), Department of
Trauma and Emergency, Indra
Gandhi Institute of Medical
Sciences, Patna, Bihar, India

A comparative study between role of platelet rich plasma (PRP) and corticosteroid injection in the treatment of osteoarthritis knee

Dr. Anand Kumar, Dr. Nand Kumar and Dr. Ashutosh Kumar

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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. Evidence on the effect of platelet-rich plasma (PRP) in treating osteoarthritis (OA) is insufficient. Therefore, the present study compares the effects of a one-time injection of PRP and corticosteroid (CS).

Methods: In the present randomized double blind clinical trial, the participants who suffered from knee osteoarthritis (Grades II/III), were randomly divided into two groups: intra articular injection of PRP and CS. Knee injury and osteoarthritis outcome score (KOOS), the 20-Meter-Walk Test (20MW), active and passive ranges of motions (ROM), flexion contracture, and pain intensity based on Visual Analog Scale (VAS) were assessed before, 2-months, and 6- months after interventions.

Results: Result evaluated based on active and passive ranges of motions (ROM), flexion contracture, and pain intensity based on Visual Analog Scale (VAS) were assessed before, 2- months, and 6-months after interventions.

Conclusions: Our study demonstrated that one shot of PRP injection, decreased joint pain more and longer-term, alleviated the symptoms, and enhanced the activity of daily living and quality of life in short-term duration in comparison with CS.

Keywords: Platelet rich plasma (PRP), corticosteroid, osteoarthritis knee

Introduction

Osteoarthritis of the knee is the most common slowly progressive chronic degenerative joint disease, characterized by varying degrees of loss of joint cartilage with local inflammation, usually affecting the elderly population [1]. There is cartilage damage combined with a significant reduction in the viscoelastic properties of the synovial fluid and the molecular weight and concentration of the naturally occurring hyaluronic acid in synovial fluid decreases. This loss of visco elasticity decreases the lubrication between joint surfaces and erodes the articular surfaces and is the mechanism of origin of pain in osteoarthritis [2]. The patient presents with pain, swelling, stiffness, deformity, decreased range of motion and disability, which significantly affect the quality of life. The knee is the most common joint that is affected in the Indian population with OA and plays an important role in weight bearing and mobility [3].

Treatment is aimed at reducing symptoms i.e. reducing pain and inflammation and maintaining performance and normal movement of the joints and slowing the progression of the disease. It includes holistic therapeutic modalities including non- pharmacological measures like patient education, physical therapy with exercises to maintain range of motion and strength, lifestyle modifications such as dieting and weight reduction, walking supports (canes/crutches), bracing, shoe and insole modification and local hot/cold fomentation [4]. Pharmacologic therapies can be in the form of oral drugs like analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and newer drugs that help in cartilage regeneration like glucosamine, and chondroitin sulfate. Topical use of NSAIDs and Capsaicin is also recommended.

Corresponding Author:

Dr. Ashutosh Kumar

Assistant Professor,
(Orthopaedics), Department of
Trauma and Emergency, Indra
Gandhi Institute of Medical
Sciences, Patna, Bihar, India

If orally administered drugs are ineffective or inadequate, Intra-articular injections (corticosteroids, viscosupplements, and blood-derived products) can be offered as another non-operative modality^[5].

When conservative measures fail, operative measures such as arthroscopic debridement, high tibial osteotomy to redistribute loading of the joint or total knee arthroplasty can be considered^[4]. OA has now become a major public health problem and a burgeoning financial burden for the global economy^[6].

Intra-articular CS has been a long-standing treatment for OA because of its anti-inflammatory and immunosuppressive effects. By acting directly on nuclear steroid receptors and interrupting the inflammatory and immune cascade, CS reduces vascular permeability and inhibit accumulation of inflammatory cells, phagocytosis, and prevents the synthesis and secretion of inflammatory mediators and increases relative viscosity and concentration of HA in the knee^[7,8,9].

HA is a natural, non-sulfated glycosaminoglycan and a component of synovial fluid that can bind to specific receptors, triggering cytokine release and stimulation of cell cycle proteins, and stimulating cell migration and proliferation^[10,11]. It acts as a lubricant of the joint and elastic shock absorber during joint movements. There is an increased susceptibility of cartilage breakdown in patients with osteoarthritis as the concentration and molecular weight of HA gets reduced^[12,13,14]. The mechanism of action of intra-articular HA injection has not been completely understood but exogenous HA is long acting and has integral roles in improving joint lubrication and synovial fluid viscosity. It inhibits proteoglycan degradation and helps in the synthesis of hyaluronan. It also has analgesic and anti-inflammatory effects^[15,16,17].

PRP is an autologous supra-physiologic concentration of platelets in a small volume of plasma, prepared by centrifugation of blood. PRP contains a 3 to 5 fold increase in platelets concentration and 1 to 25 fold higher concentration of cytokines and growth factors that are capable of stimulating cellular growth, vascularization, proliferation, tissue regeneration, and collagen synthesis^[18]. The release of platelet-derived factors directly at the site of cartilage disease, particularly with interest to knee OA, may stimulate the natural regenerative signaling cascade and enhance the healing of tissue with further mediation of the anti-inflammatory response^[19].

The aim of the present study was to evaluate and compare the efficacy of intra-articular corticosteroid injections with PRP for the treatment of knee OA.

Materials and Methods

This prospective randomized study was conducted in the outpatient department of Darbhanga Medical College & Hospital after approval of the institutional ethics committee, from December 2018 to September 2020. 82 patients (138 knees) of either sex, between 40 and 70 years of age, suffering from primary knee OA with Kellgren and Lawrence (KL) Grade II or III on standing antero-posterior and lateral knee radiographs^[20], with symptoms for more than 3 months according to the ACR clinical classification criteria^[21] and pain score of more than 4 cm on 10 cm visual analog scale (VAS) were included in this study. Written informed consent was obtained from all patients before treatment.

Patients with history of significant trauma to the affected knee, active infection or tumors around the knee, secondary OA; having diabetes mellitus, cardiovascular diseases, coagulopathies, immunosuppressive, collagen, or autoimmune

disorders or having a prior history of knee injections, hemoglobin values of <10 g/dl or platelet values of <150,000/ml; those receiving treatment with anticoagulant or anti-platelet medications or systemic corticosteroids 10 days before injection or recent use of NSAIDs; and pregnant and breastfeeding females were excluded from the study^[4].

20 ml of venous blood was drawn from the antecubital vein using an 18G needle to avoid traumatizing platelets and was collected in a sterile tube containing 2 ml of Sodium Citrate anticoagulant. Approximately 2 ml of whole blood was separated for a complete blood count^[4]. The blood with anticoagulant was centrifuged at 4000 rpm for 6–10 minutes to separate erythrocytes and then at 4000 rpm for 6–10 min to concentrate platelets. The final product was 4–5 ml of PRP-containing leukocytes with platelet concentration of 3–5 times the average normal value.

In all, 82 patients were randomly divided into 2 equal groups by random allocation sequence using a random-numbers table. The first group included 40 patients who were treated with one intra-articular injection of 2 ml of methylprednisolone acetate at 40 mg/ml mixed with 2 ml of lignocaine. The second group included 42 patients who were treated with a single 5 ml intra-articular injection of PRP prepared in our hospital.

Before the administration of each injection, knee effusions if present, were aspirated into a separated syringe; the same needle was left in place and the syringe prefilled with CS or PRP was used for injection^[21].

The injection was given at a site near the superolateral pole of patella in the suprapatellar pouch under aseptic conditions^[4], with knee kept in 15–20 degree flexion and the patient was advised to take 1 day of rest after injection and apply ice to the area if there were any signs of inflammation^[21].

The Western Ontario and McMaster University Osteoarthritis Index (WOMAC) and the 10 cm visual analog pain scale were used to assess the response to treatment at various intervals. The WOMAC was used as a self-administered test consisting of a 24-item questionnaire divided into three subscales which measure pain (5 items, score range 0–20), stiffness (2 items, score range 0–8), and physical function (17 items, score range 0–68)^[22]. The three normalized subscale values were summed to provide the normalized WOMAC-total score in the range of 0 (best score) to 96 (worst score). With the use of WOMAC, a lower score represented a better outcome^[23].

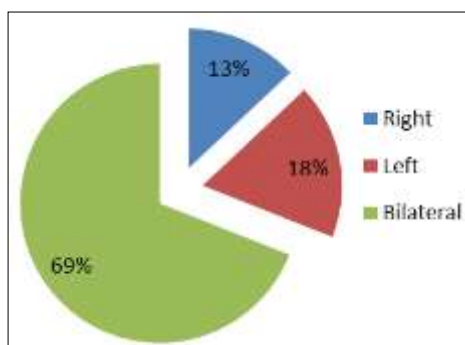
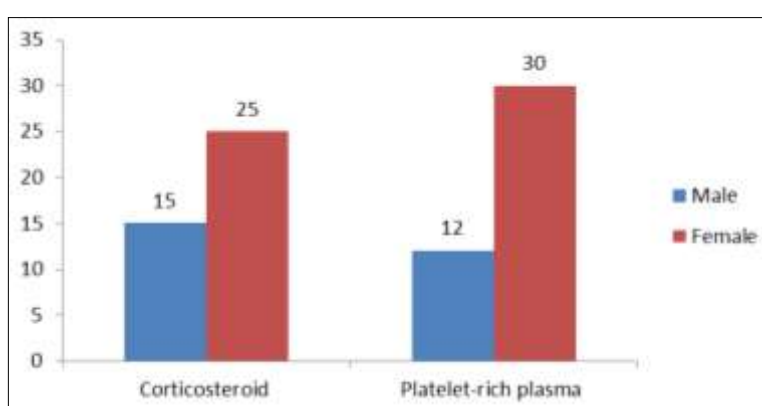
The VAS, which also was administered by the patient, ranged from 0 to 10 cm, with lower numbers representing less pain and higher numbers representing more pain^[21]. All the three measurements were used at the time of enrollment in the study before any injection and then the VAS was measured again at six weeks three and six months follow-up while the WOMAC was also measured at six weeks three and six months. The measurements were recorded in a proforma and tabulated.

Results

Among the 82 patients enrolled in our study, 27 (32%) were male and 55 (68%) were female with a mean age of 64.7. Out of 82 patients, there were 26 unilateral knee cases and 56 bilateral knee cases. A patient with bilateral knee pain was considered as one patient. 11 (13%) patients had OA on the right knee and 15 (18%) on the left knee, and the remaining 56 (68%) had bilateral knee involvement. The mean age of the patients in the corticosteroid group were 64.7 ± 9.1 years and in platelet-rich plasma group were 63.8 ± 9.4 years. Males constituted 37.5% in corticosteroid group and 28.5% in platelet-rich plasma group.

Table 1: Sex wise distribution of patients in the study groups

	Corticosteroid		Platelet-rich plasma	
	Number	Percentage	Number	Percentage
Male	15	37.5	12	28.5
Female	25	62.5	30	71.5

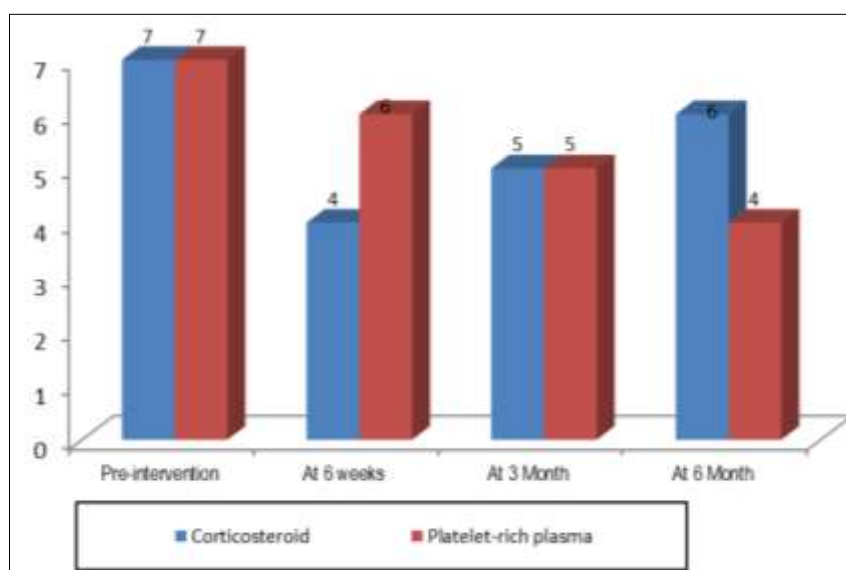
**Fig 1:** Percentage wise distribution of involved limbs in the study groups**Fig 2:** Percentage distribution of male and female patients in the two study groups**Pain (VAS)**

The VAS score before intervention in corticosteroid group was 7 ± 2 and in platelet-rich plasma group was 7 ± 2.5 . In corticosteroid group, pain at end of six weeks significantly decreased to 4.5 ± 1.5 . At the end of three months, pain increased to 5 ± 2 and at the end of six months, pain score increased to 6 ± 2 . In platelet-rich plasma group, at end of six months, pain significantly decreased to 6 ± 2 , pain continued its decreasing trend to 5.5 ± 1.5 at end of third month. At the

end of six month, pain score decreased to 4 ± 2 and it was also significantly lower than primary pain score.

Table 2: Comparison of VAS scores between the study groups at pre-intervention and 1, 2 and 3 months post-intervention

VAS score	Pre-intervention	At 6 weeks	At 3 month	At 6 month
Corticosteroid	7 ± 2	4.5 ± 1.5	5 ± 2	6 ± 2
Platelet-rich plasma	7 ± 2.5	6 ± 2	5.5 ± 1.5	4 ± 2

**Fig 3:** Comparison of VAS scores between the study groups at pre-intervention and 1, 2 and 3 months post-intervention

WOMAC score

Pain and stiffness in the two study groups decreased 3 months after intervention. Also physical function significantly improved in the two groups. The improvement was more significant in PRP group as compared to corticosteroid and platelet-rich plasma groups at the end of 3 months.

Table 3: Shows PRP group as compared to corticosteroid and platelet-rich plasma groups at the end of 3 months

WOMAC score	Corticosteroid		Platelet-rich plasma	
	Mean	SD	Mean	SD
Before injection	78.5	10.5	78.5	10.5
At 6 weeks	72.5	8.5	74.5	8.5
At 12 weeks	68.5	8.5	66.5	10.5
At 24 weeks	55.5	10.5	52.5	10.5

Discussion

Primary treatment goals in knee OA include pain reduction and improvement of joint mobility and function. The secondary goal is to decrease the progression of disease. Platelet rich plasma is a non-operative intervention, which is frequently administered with the hope of achievement of both primary and secondary therapeutic goals over longer duration as compared to corticosteroid. These two categories of intra-articular injections need to be clinically evaluated comparatively to assign their indications, contra-indications and to determine which treatment method was more effective for alleviation of pain and durability.

This study showed that in the two study groups, the functions of the knee improved, but intra-articular PRP injection were found superior to corticosteroid in improving pain, stiffness, and functional status over a longer term.

VAS scale showed that two modalities were effective in pain reduction at six weeks, third and six month after intervention. The effectiveness of pain reduction was more durable in PRP group as compared to CS. The pain score gradually increased at the six month endpoints after decreasing drastically at the six month and three month endpoint but still remained better than pre-intervention levels in CS group.

WOMAC Scores showed improvement in all the parameters post-intervention after 3 months. The improvement was more significant in PRP group as compared to corticosteroid group at the end of 3 months providing a good clue to compare the clinical efficacy of each intervention over 3 months.

Since the degree of pain relief was comparable across the study groups; consequently, it is argued that the most important difference between the two intervention modalities is the duration of effectiveness. Compared to CS group, PRP is suggested to be superior in the duration of pain relief. We can propose that intra-articular PRP injections provide significant pain relief even after 3 months post-intervention and the need for re-administration is less likely as compared to CS after every 3 months for knee joint OA.

None of the patients were lost during follow-up. We found that conducting studies with more extensive follow-ups and significantly larger sample size was demanding. In a prospective, randomized study, by Jones *et al.* patients withdrew during follow-up most commonly because of worsening of the symptoms over a longer term of conservative treatment thus challenging the utility of conservative methods of treatment of OA knee over a longer duration.

Conclusion

In the treatment of moderate OA when physical therapy and other pharmacological therapy fails to relieve pain then intra

articular injection can be used, as short term measure. It is safe and effective. Though it is not a permanent solution for knee OA but it relieves pain. Improve function and quality of life. In acute exacerbation of pain. Intra articular steroid can be given, it relieves pain rapidly and its effect lasts for 8-10 weeks. Intra articular PRP comparatively gives longer duration of pain relief. PRP is more effective in relatively younger age patients and lower degree of cartilage degeneration.

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