

Study of functional outcome of intra articular platelet rich plasma injections in early osteoarthritis knee

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Abstract

Background: Osteoarthritis (OA) is a chronic disorder of synovial lined joints, due to an imbalance between normal cartilage derivative and repair mechanisms. Different methods are used to alleviate the symptoms of patients with knee OA, including analgesics, physical therapy, exercise, intra-articular injections (glucocorticoids, hyaluronic acid, etc.) and use of platelet-rich plasma (PRP), as an autologous growth factor treatment. The purpose present study was to assess the effectiveness of intra-articular platelet-rich plasma (PRP) injections in patients with OA knee in terms of pain and functional handicap. **Material and Methods:** Present study was a prospective, interventional study conducted in patients 30-70 years, with knee osteoarthritis, knee pain for more than 6 months and not responding to analgesics and exercises, willing to participate and follow up. **Results:** Total 60 patients (80 knees) were included for present study. 51-60 years age group was most common (44%), followed by 41-50 years age group (28%). Female (55%) were more than male (45%). Other common factors were BMI > 30 kg/m² (45%), postmenopausal female (36%) and diabetic patients (18%). Patients were evaluated using Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Score (VAS) at day 1, at the end of 1st, 3rd, 6th and 12th month on follow up. Significant reduction in WOMAC Score and VAS Score was noted during follow up. A statistically significant difference was noted in WOMAC Score and VAS Score for preinjection and at 6 months values. In all grades of osteoarthritis, reduction in WOMAC score and VAS Score was noted at 6 months follow up. In grade 1,2 and 3 statistically significant difference was noted for preinjection and at 6 months values, while in grade 4 patients' difference was not significant. **Conclusion:** A single PRP intra-articular injection is effective for relieving pain and improving activity of daily living and quality of life in patients with knee OA.

Keywords: platelet rich plasma, osteoarthritis, knee joint, Visual Analogue Scale (VAS), West Ontario McMaster (WOMAC) score.

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INTRODUCTION

Osteoarthritis (OA) is a chronic disorder of synovial lined joints, due to an imbalance between normal cartilage derivative and repair mechanisms, which results in net cartilage loss, hypertrophy of bone, and osseous outgrowths called osteophytes.¹ The most common symptoms of knee osteoarthritis are pain and physical limitations that have a significant effect on the individual's quality of life and her or his social and economic activities. Different methods are used to alleviate the symptoms of patients with knee OA, including analgesics, physical therapy, exercise, intra-articular injections

(glucocorticoids, hyaluronic acid, etc.) and use of platelet-rich plasma (PRP), as an autologous growth factor treatment. If these procedures fail, then more invasive surgical approaches can be attempted to avoid metal resurfacing through the restoration of the mechanical balance and the regeneration of the articular surface, though the results are still controversial.²

Nonsteroidal anti-inflammatory drugs (NSAIDs), commonly prescribed medications only provide symptomatic relief rather than eradicating the disease. In addition, they pose an increased risk for cardiovascular diseases, stroke, gastrointestinal and renal complications.³ Some studies have considered using intraarticular injection (IAI) as a first-line treatment because it has proven effectiveness for relieving pain with fewer adverse effects than some oral medications.⁴ American Academy of Orthopaedic Surgeons clinical practice guidelines have demonstrated inconclusive evidence to recommend for or against corticosteroid and strong evidence against hyaluronic acid (HA) visco-supplementation injections for patients with symptomatic knee OA.⁵ The purpose present study was to assess the effectiveness of intra-articular platelet-rich plasma (PRP) injections in patients with OA knee in terms of pain and functional handicap.

MATERIAL AND METHODS

Present study was a prospective, interventional study conducted in Department of Orthopaedics, Geetanjali Medical College and Hospital, Udaipur,. Study was conducted between July 2019 to June 2020 (1 year). Study was approved by institutional ethical committee. Patients diagnosed with knee osteoarthritis were considered for present study.

Inclusion criteria

Patients 30-70 years, with knee osteoarthritis, knee pain for more than 6 months and not responding to analgesics and exercises, willing to participate and follow up.

Exclusion criteria

- Osteoarthritis secondary to inflammatory joint disease.
- Patients with other diseases, affecting the knee joint chondrocalcinosis, acute synovitis, excessive joint effusion (>100 ml), cystic diseases around the knee joint (e.g. Popliteal cyst)
- Relative contraindications pertaining to platelet concentrate use - history of thrombocytopenia, use

of anticoagulant therapy, active infection, tumour, metastatic disease.

- Infection in and around knee, history of severe trauma to the knee,
- Collagen vascular diseases, any malignant disorders, clotting disorders, taking anticoagulant and antiplatelet medications,
- History of intraarticular knee injections of corticosteroids,
- Lost to follow up

Study was explained to patients in local language and written informed valid consent was taken. Each patient was examined clinically and radiographically along with detailed demographic data compilation. CBC, PT/INR and X-rays of bilateral knees were done. Radiological grading was done using Kellgren–Lawrence (KL grading) OA scale. 30 mL of whole blood was collected from the arm. From the drawn venous blood, PRP is separated by two-step centrifugation as per standard procedure. The resulting buffered platelet concentrate contained approximately 6 to 8 times concentration of platelets compared to baseline whole blood. In operation theatre, cleansing of the patient's skin around the injection site was done; towels or drapes were used to create an aseptic field. Administration of a local anesthesia was done. With sterile technique, PRP was injected intraarticularly into the knee; and dressing or bandage was applied to protect the needle entry site. Immediately after the injection, the patient was kept in sitting position without moving the knee for 15 minutes. Patients were started with static quadriceps, static hamstrings, ankle toe movements, and knee range of movement exercises. A strict vigilance was done in view of adverse reactions such as pain following injection, joint swelling or any systemic reaction. If patient experiences pain, ice pack application given, if not subsided opioid analgesics were given for pain. Patients were evaluated using Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Score (VAS) at day 1, at the end of 1st, 3rd, 6th and 12th month on follow up. Statistical analysis was done using SPSS version 21. All score values were summarized in the form of means and standard deviation (SD). To compare the change in the WOMAC score/ VAS scores at 6 weeks from baseline in terms of KL grade, Student's t-test and/or ANOVA test was used to calculate the p-value. p-value less than 0.05 was considered as statistically significant.

RESULTS

Total 60 patients (80 knees) were included for present study. 51-60 years age group was most common (44%), followed by 41-50 years age group (28%). Female (55%) were more than male (45%). Other common factors were BMI > 30 kg/m² (45%), postmenopausal female (36%) and diabetic patients (18%).

Table 1: General characteristics

Characteristics	Number of cases	Percentage (%)
Age (years)		
≤ 40	5	6%
41-50	22	28%
51-60	35	44%
61-70	18	23%
Mean ± SD (years)	50.79 ± 9.14 years	
Gender		
Male	36	45%
Female	44	55%
Other factors		
BMI > 30 kg/m ²	36	45%
Postmenopausal female	29	36%
Diabetic	14	18%

Patients were evaluated using Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Visual Analogue Score (VAS) at day 1, at the end of 1st, 3rd, 6th and 12th month on follow up. Significant reduction in WOMAC Score and VAS Score was noted during follow up. A statistically significant difference was noted in WOMAC Score and VAS Score for preinjection and at 6 months values.

Table 2: WOMAC and VAS scores

Score	Pre-injection	6 weeks	3 months	6 months
WOMAC Score (Mean ± SD)	59.32 ± 6.13	48.23 ± 5.67	43.57 ± 7.44	37.11 ± 9.29
VAS Score (Mean ± SD)	6.45 ± 2.16	4.24 ± 1.52	3.67 ± 1.36	3.22 ± 1.27

In all grades of osteoarthritis, reduction in WOMAC score was noted at 6 months follow up. In grade 1,2 and 3 statistically significant difference was noted for preinjection and at 6 months values, while in grade 4 difference was not significant.

Table 3: OA grade specific WOMAC scores

KL Grade	No. of patients (%)	Pre-injection	6 weeks	3 months	6 months
1	16 (20%)	32.82 ± 5.56	23.35 ± 5.13	17.55 ± 4.36	17.57 ± 5.36
2	29 (36%)	39.58 ± 6.56	25.69 ± 5.37	21.65 ± 4.25	24.57 ± 3.44
3	24 (30%)	51.23 ± 6.66	40.56 ± 5.67	29.53 ± 5.42	31.38 ± 6.71
4	11 (14%)	68.29 ± 7.34	64.32 ± 6.12	61.44 ± 4.93	64.46 ± 6.13

In all grades of osteoarthritis, reduction in VAS score was noted at 6 months follow up. In grade 1,2 and 3 statistically significant difference was noted for preinjection and at 6 months values, while in grade 4 difference was not significant.

Table 4: OA grade specific VAS scores

KL Grade	No. of patients (%)	Pre-injection	6 weeks	3 months	6 months
1	16 (20%)	4.55 ± 1.21	2.81 ± 1.35	2.11 ± 0.57	2.32 ± 0.91
2	29 (36%)	5.67 ± 1.02	3.89 ± 1.01	3.35 ± 0.73	3.54 ± 1.01
3	24 (30%)	6.34 ± 0.91	4.74 ± 1.23	3.42 ± 1.00	3.58 ± 1.03
4	11 (14%)	7.13 ± 1.23	6.54 ± 1.09	6.31 ± 0.89	6.69 ± 0.98

5 patients had mild pain and effusion after the injection, which was managed conservatively. No infection, marked muscle atrophy, deep vein thrombosis, fever, hematoma, tissue hypertrophy, adhesion formation, or other major adverse events occurred among study subjects.

DISCUSSION

Individuals affected with osteoarthritis clinically presents with deep aching joint pain, joint swelling, and reduced joint range of motion and crepitus of joint. Weight bearing anteroposterior and lateral radiograph may show narrowing of joint space, osteophyte formation, subchondral cyst and sclerosis.^{6,7} Due to the increase in life

expectancy, the number of elderly people, and the prevalence of obesity in society, it seems that the prevalence of knee osteoarthritis will increase. Platelet-rich plasma (PRP) classically described as “a volume of plasma that has a platelet count above baseline” indicates a concoction of plasma (the cellular, liquid portion of the blood containing proteins responsible for clotting and other

bioactive molecules playing a significant role in wound repair) and platelets (and their associated growth factors and cytokines).⁸ Platelet-rich plasma (PRP) is an autologous derivative of whole blood that contains high concentrations of growth factors including transforming growth factor- β , insulin-like growth factor, platelet-derived growth factor, basic fibroblast growth factor, and vascular endothelial growth factor, as well as bioactive proteins that influence the healing of tendon, ligament, muscle, and bone.⁹ In present study, OA was more in women compared to men. This difference can be possibly due to the lack of physical activity, mobility, obesity, social issues in general. OA strikes women more often than men and it increases in prevalence after menopause. Similar observations were noted by Sharma *et al.*¹⁰ and Maheshwari P¹¹. In study by Maheshwari P¹¹, they noted that low grade OA knee (KL grade 1, 2, 3) have better outcomes as compared to higher grade OA knee (KL grade 4) as well as younger age group (50-55 years) has lower WOMAC. Gobbi *et al.*¹² tried to determine the effectiveness of intra-articular PRP injections in active patients with knee OA and to evaluate clinical outcomes in patients with and without previous surgical treatment for cartilage lesions. The PRP treatment showed positive effects in patients with knee OA. Operated and non-operated patients showed significant improvement by means of pain reduction and improved symptoms and quality of life. Hemeshwar *et al.*,¹³ noted that all patients had significant improvement in WOMAC score and VAS score at 1, 3, 6 and 12 months (P value < 0.05) except grade 4 OA. Similar findings were noted in present study. Chitharth R *et al.*,¹⁴ studied 50 knees and followed up at 1st, 3rd and 6th month. The mean baseline VAS was 7.48, which was found to be significantly reduced at the end of follow up to 3.6 (48.1% reduction in pain). Mean total WOMAC score initially at baseline was 79.58 and at the end of the study was 37.66 with significant reduction. From the third month of follow up, there was significant improvement of VAS score and WOMAC score. In a double blinded randomized controlled study, in patients of bilateral early osteoarthritis knee, injected PRP in one knee and normal saline in other knee serving as physiological control. noted decrease in mean pain score after 2 weeks of injection in PRP knee. Pain relief was 24% and 50% at 2nd week and 3rd month respectively. In NS knee, no improvement of pain was seen in VAS scale at 2nd week, 1.5th month and 3rd month. At 6 months, pain reduction in PRP knee was 49%, as compared to only 21% decrease in NS knee.¹⁵ Several studies have investigated the effects of leukocyte-poor versus leukocyte-rich PRP in tissue healing. PRP rich in leukocytes have been shown to cause a significantly greater acute inflammatory response and increased synovial cell death.^{16,17} In patients with symptomatic

knee OA, PRP injection results in significant clinical improvements up to 12 months postinjection. Clinical outcomes and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores are significantly better after leukocyte-poor PRP versus hyaluronic acid at 3 to 12 months postinjection.¹⁸ Multiple placebo-controlled studies have shown that IA injection of platelet-rich plasma (IA PRP) can relieve pain, improving knee function and quality of life. The most likely mechanism by which PRP reduces pain and stiffness of OA is by stimulating the natural healing cascade and tissue regeneration by a “supra-physiological” release of platelet-derived factors directly at the site of treatment.^{19,20,21} PRP acts at various levels to alter the joint homeostasis. In cartilage it decreases catabolism, improves anabolism and promotes chondral remodeling. Higher amounts of prostaglandin (PG) and collagen II synthesis, increasing chondrocyte proliferation and production of matrix molecules have also been observed.²² Moreover, since articular cartilage is not innervated, approximately 50% of the patients with radiological changes of OA are symptomatic; therefore, the treatment is based on symptoms rather than radiological changes. OA is a joint failure and not just cartilage tissue disorder, disease-modifying agents in OA treatment would more likely to succeed if they focused primarily on correcting the abnormal mechanics and then addressing the cartilage loss if needed.²³ Limitations of this study were relatively small number of patients involved, short-term follow-up after PRP injections and no control group. Further studies with large sample, comparative studies with long follow-up period to evaluate the role of PRP injections are needed.

CONCLUSION

This study has concluded that amount of pain relief, and improvement in function in individuals with OA during the first 6 months after starting the PRP treatment. A single PRP intra-articular injection is effective for relieving pain and improving activity of daily living and quality of life in patients with knee OA.

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