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ORIGINAL ARTICLE

Intra-articular Injection of Platelet-rich Plasma *vs.* Local Anesthetic with Steroid to Treat Knee Osteoarthritis: A Prospective Randomized Controlled Study

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ABSTRACT

Introduction: Osteoarthritis (OA) of the knee is a prevailing, chronic degenerative condition that generates a high expense. Alternative and adjuvant therapies are currently being foraged to improve the physical function and quality of life of affected patients. Intraarticular (IA) corticosteroid injection provides a short-term reduction in OA knee pain. Platelet-rich plasma (PRP) is now an emerging modality for OA knee, but there is still a lack of clinical evidence.

Aim: To evaluate the clinical effectiveness of knee IA injection of corticosteroid + local anesthetic (LA) with that of autologous PRP using standard scoring systems. To assess the degree of pain relief, improvement in range of motion of the knee joint and incidence of adverse effects.

Materials and methods: Sixty-four patients selected according to the inclusion criteria were treated with two IA injections given 4 weeks. All patients were divided into two groups–group P and S. Thirty two patients in group P were treated with PRP and 32-patients in group S with LA + Steroid. All patients were prospectively evaluated at the pain clinic and 3 and 6 months after the treatment for the following parameters: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, index of severity for knee osteoarthritis (ISK) score by Lequesne et al., visual analog score (VAS) score and range of motion of knee. Adverse events were also chronicled.

Results: There was an improvement in both the groups at 3 months, but there was no statistically significant difference between the ISK scores, MWI scores, and ROM whereas VAS score in group S was significantly lower than group P (*p* value = 0.03). At 6 months follow-up, the mean VAS score, the ISK scores, MWI scores and ROM in the group P were significantly lower than group S (*p* value = 0.0001; 0.0001; 0.003; 0.001). No significant complications related to injection were observed during the treatment and follow-up.

Conclusion: Improvement in the knee function was better with PRP than steroid group at short term follow-up. PRP is safe and more effective than steroids in alleviating pain in symptomatic OA knee.

Keywords: Chronic pain, Intra-articular injection, Osteoarthritis knee, Platelet-rich plasma, Steroids.

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INTRODUCTION

Osteoarthritis, being the most common disease of the joints in the elderly, frequently affects the knee joint causing a major source of disability owing to pain and significant loss of function.[1]

Recently there has been a stronger emphasis placed on developing new modalities that aim to slow the disease progression or even reverse the process in OA knee. IA injectables ranging from the traditional use of corticosteroids to more recent PRP and stem cells are being used to manage OA knee.[2] IA corticosteroids provide a short-term reduction in the pain and can be considered as an interim solution for the relief of moderate to severe OA knee pain.[3] PRP represents a user-friendly therapeutic measure that shows encouraging preliminary clinical results in active patients with OA knee. PRP stimulates the natural healing cascade and tissue regeneration by a "supraphysiologic" release of platelet-derived growth factors directly at the site of treatment.[1,4,5]

Our prospective randomized study was designed to compare the safety and efficacy of IA PRP with that of corticosteroid for OA knee.

AIM AND OBJECTIVES

Primary Objective

To evaluate the clinical effectiveness of intraarticular knee injection using standard scoring systems.

Secondary Objectives

- To evaluate the degree of pain relief.
- To assess the improvement in range of movement of the knee joint.
- To study the incidence of adverse effects.

MATERIALS AND METHODS

After taking ethical committee approval, the study was conducted on the patients visiting the Pain Relief Centre at JSS Hospital fulfilling the inclusion criteria (Table 1).

A total of 64 patients with H/O chronic knee pain ≥3 months with VAS score >4 and X-ray knee showing degenerative changes of the joint (KL grade 1–3), who met the inclusion criteria were selected. All patients were randomized by simple random sampling, serially numbered opaque sealed envelope (SNOSE) technique and allocated into two equal groups.

- *Group P*: Received 5 mL of knee IA injection of autologous PRP
- *Group S*: Received 5 mL of knee IA injection of LA+ Steroid (1 mL of triamcinolone acetonide 40 mg + 4 mL of 0.25% bupivacaine).

The PRP was prepared and provided by the double spinning method using REMI R-8C BL machine by the Department of Transfusion Medicine, JSS medical college (JSSMC), Mysuru. All the patients were treated with two IA injections (4 weeks apart) and followed up. IA injections were performed on an outpatient basis under aseptic precautions and ultrasound guidance by the investigator, who was not involved in the assessment of the patients. After injection, patients were sent home with instructions to restrict the use of the leg for 24 hours and to use cold/ice therapy for knee if there was a pain. Assessment of all the parameters mentioned below was done at each subsequent follow-up visit by the evaluator, not involved in the intervention. The only permitted medication throughout the study period was acetaminophen. Adverse effects like pain, swelling, redness and infection were also recorded at each follow-up visit. The following parameters were recorded at the first basal visit and at subsequent follow-up visits at 3 and 6 months after the last injection:

- Modified WOMAC index (MWI) score (Modified – CRD Pune Version)
- Index of Severity for Knee Osteoarthritis (ISK) by Lequesne et al.
- VAS score
- The range of motion using a goniometer

Table 1: Inclusion and exclusion criteria

Inclusion criteria	*Exclusion criteria*
• AGE: 18–75 years • History of (H/O) chronic knee pain (at least 3 months) VAS score >4 • Patients with Kellgren–Lawrence (KL) grade 1 to 3 (X-ray knee of the patient in standing position showing degenerative changes of the joint)	• Patients with H/O trauma to the knee joint, polyarticular disease, KL score >3, • H/O systemic autoimmune rheumatoid disease • H/O Coagulopathy, Bleeding disorders • Patients on Anticoagulants, Anti-platelet drugs. • H/O previous knee surgery • Hb <11gm/dL, Platelet count <150,000/mm^3

Statistical Analysis

The data obtained were analyzed using the Statistical Package for the Social Sciences (SPSS) 21.0 version. All continuous data were expressed in terms of the mean and the standard deviation of the mean. To assess the differences in the mean of the two groups, T-test was performed. Repeated measures of continuous variables, repeated measure analysis of variance (ANOVA) was done for within group. Two way repeated measure ANOVA done for between groups difference over time. The non-parametric Pearson's Chi-square test was performed to investigate the relationships between grouping variables. For all these tests, $p < 0.05$ was considered significant.

RESULTS

Both the groups were comparable in Age, Sex, BMI and KL grading (Table 2).

The baseline MWI score (p value = 0.9) , ISK score (p value = 0.1), VAS score (p value = 0.3) and ROM (p value = 0.5) were also comparable with no significant difference between both the groups (Table 3).

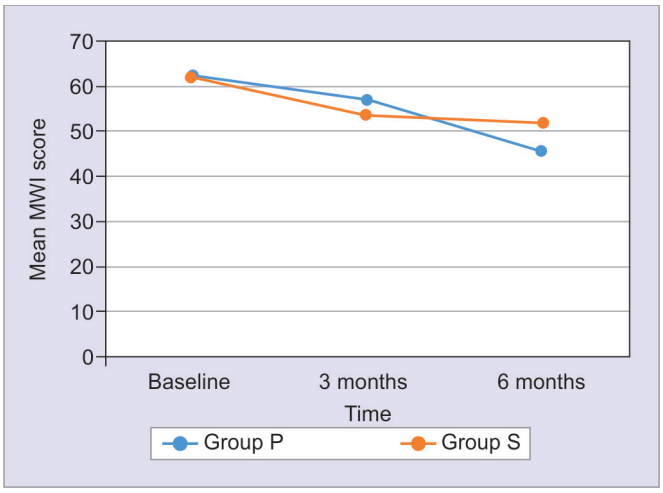
The mean MWI score at three months follow-up in the group P was 57.12, while that in the group S was 53.59 with no statistically significant difference between both the groups (p value = 0.6). But at the six months follow-up, the mean MWI score in the group P is 45.12, while that in the group S is 51.41. The MWI scores of the group P are significantly lower when compared to that of the group S (p value = 0.003) (Graph 1 and Table 3).

The mean ISK scores at three months follow-up in the group P was 13.50, while that in the group S was 13.63, suggesting that there was no statistically significant difference between both the groups (p value = 0.8). But at six months follow-up, the mean ISK score in the group P was 11.06 which was lower compared to that of the group S score 13.28 (p value = 0.001) (Graph 2 and Table 3).

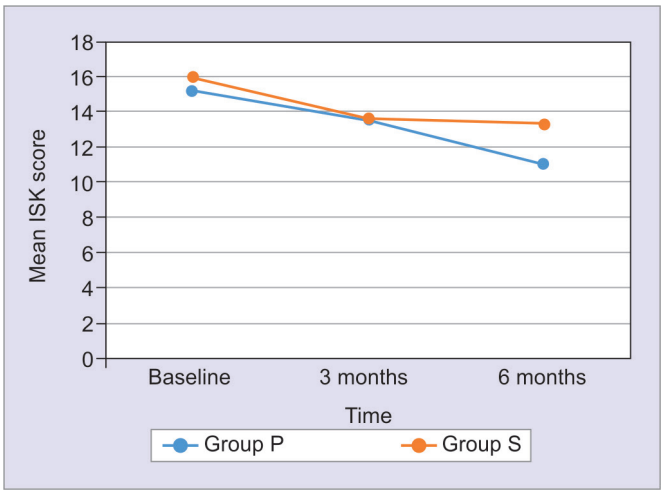
The mean VAS score at three months in the group S was 4.53 which was lower than in the group P, i.e., 5.00 (p value = 0.03). But at six months follow-up, the mean VAS score in the group P was 3.66, was much lower than that of the group S–4.72, with high statistical significance (p value = 0.0001) (Graph 3 and Table 3).

Table 2: Demography, BMI and KL grading of the two groups

	Group P	*Group S*	*p value*
Age in years	49 ± 7.0	49.6 ± 7.9	0.7
Sex (%)–	50%	46.9%	0.8
Female	50%	53.1%	
Male			
BMI in kgm^{-2}	24.94 ± 2.09	24.19 ± 1.60	0.1
KL Grade			
1	15.6%	15.6%	
2	43.8%	34.4%	0.7
3	40.6%	50%	



Graph 1: Mean MWI scores at follow-ups between the two groups



Graph 2: Mean ISK scores at follow-ups between the two groups

Table 3: Baseline and follow-up parameters

Parameters	*Group P*	*Group S*	*p value*
MWI Score			
Baseline	62.28 ± 8.41	62.13 ± 7.0	0.9
3 months	57.12 ± 7.3	53.59 ± 7.64	0.6
6 months	45.72 ± 6.25	51.41 ± 8.29	0.003
ISK Score			
Baseline	15.19 ± 1.99	15.97 ± 1.93	0.1
3 months	13.50 ± 1.68	13.63 ± 1.90	0.8
6 months	11.06 ± 1.50	13.28 ± 1.92	0.0001
VAS Score			
Baseline	6.13 ± 0.55	6.28 ± 0.58	0.3
3 months	5.00 ± 0.98	4.53 ± 0.62	0.03
6 months	3.66 ± 0.79	4.72 ± 0.73	0.0001
ROM (in degrees)			
Baseline	90.00 ± 11.07	88.13 ± 9.98	0.5
3 months	93.33 P ± 10.66	93.44 ± 9.02	0.1
6 months	110.00 ± 11.07	99.06 ± 9.95	0.001

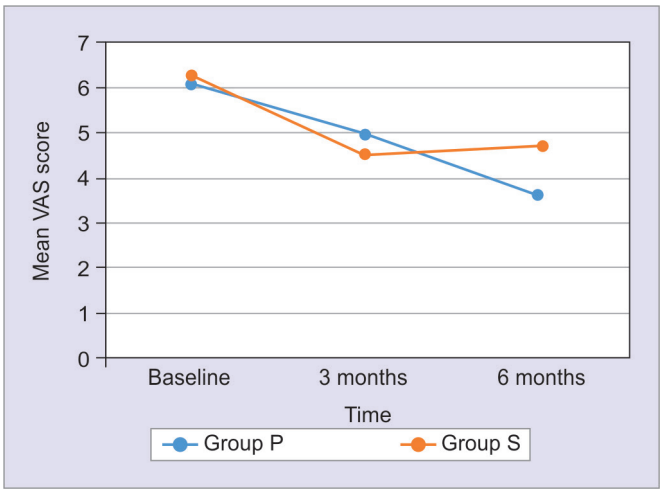
The mean ROM in the group P at 3 months follow-up was 93.33, while that in the group S was 93.44 (p value = 0.1); denoting that there is no significant difference between both the groups. But at six months follow-up ROM in the group P was 110.00 while in the group S it was 99.06 with a significantly higher value in group P (p value of 0.001). At six months follow-up there was an improvement of ROM in both the groups with group P better than group S (Graph 4 and Table 3)

There were minor adverse effects reported in 3 patients (2 in the PRP group and 1 in the steroid group) in the form of an increase in pain and swelling within 48 hours of intraarticular injection. However, this reaction was self-limiting within a few days and did not affect the overall outcome in those patients.

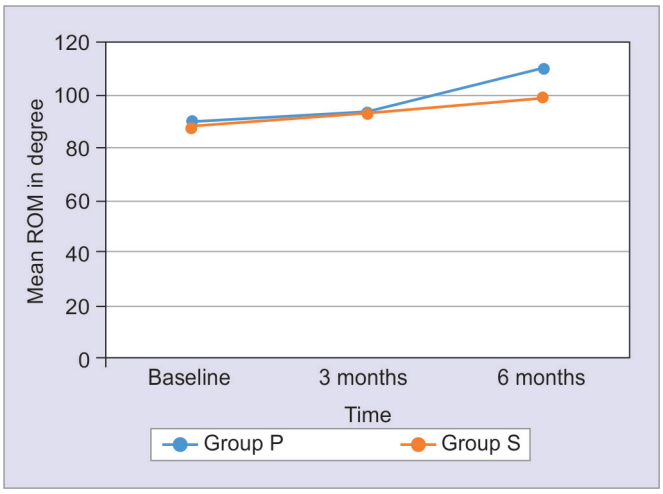
DISCUSSION

The OA knee is one of the main causes of musculoskeletal disability. With the increasing aging population and drift in the prevalence of obesity, it is expected that the burden of OA on the population, healthcare system, and the overall economy will continue to increase.[2,6]

Current literature indicates that IA knee injection is a promising modality in managing pain associated with OA knee. It is a well tolerated, minimally invasive



Graph 3: Mean VAS scores at follow-ups between the two groups



Graph 4: Mean ROM (in degrees) at follow-ups between the two groups

intervention, especially in patients with co-morbidities, who neither have the fitness for the surgery nor able to tolerate oral analgesics for a long-term period. Various IA injectables like corticosteroids, infliximab, hyaluronic acid, botulinum neurotoxin, PRP, and even stem cells are being used in the management of knee OA.[7-10]

A single-injection hyaluronic acid gel (Durolane–Bioventus) and an extended-release (ER) formulation of the synthetic corticosteroid triamcinolone acetonide (Zilretta–Flexion) has gathered FDA approval for IA treatment of osteoarthritic knee pain.[11]

Traditionally IA steroids are used for OA knee pain. Steroids act on nuclear steroid receptors and heckle the inflammatory and immune cascade at several levels. Last few years, there is growing interest in exploring PRP as a treatment modality for OA knee. The platelet concentrate in PRP when activated results in the formation of platelet gel and the release of growth factors and bioactive molecules which effectively participate in the healing process.[12] There are numbers of ongoing studies about the effects of PRP on OA knee. Till date, there is no concurrence on the number of injections, the most effective platelet concentration and the repercussions of long-term PRP.[13]

Despite its widespread use and the positive findings reported in the clinical practice, there is a lack of scientific credentials to guide the clinical application of PRP. As we did not find literature regarding studies comparing the effectiveness of PRP with that of most commonly administered IA steroids, we decided to conduct this clinical study.

Among the steroids, triamcinolone acetonide is one of the most commonly used drugs for IA injections. The studies by so many authors like Arden et al.[14,] Chao et al.,[15] Raynauld et al.,[16] Beyaz et al.[17] have used triamcinolone acetonide as the steroid drug in the dose of 40 mg for IA injections in OA knee. The same was followed in our study.

The efficacy of intraarticular corticosteroids in knee OA has been confirmed in a Cochrane review done in 2006, and in a systematic review by Hepper et al.[18] and a meta-analysis by Bannuru et al.[19] Chao J et al.[15] found IA corticosteroids to be superior to placebo on WOMAC scores at four weeks. Arroll et al.[20] and Arden et al.[14] suggested a benefit at twenty-six weeks, which was similar to our study.

Beyaz et al.[17] had used 40 mg of triamcinolone acetonide and 4 mL of 0.25% Bupivacaine for IA injection and reported a significant improvement in VAS scores and WOMAC scores till three months of their follow-up period. Our results were similar to their study. The research evidence demonstrates that IA corticosteroid injections provide a short-term reduction in OA pain.

The clinical trials conducted in the past few years resonate the growing interest in exploring PRP as a treatment modality in the OA knee. Sánchez et al.[21] were the first to describe the IA injection of plasma rich in growth factors for treating articular cartilage avulsion in a soccer player. The studies by Sampson et al.,[22] Kon et al.,[23] Spaková et al.,[24] Say et al.,[25] Patel et al.[26] reported a favorable outcome with IA injections of PRP in most of the OA knee patients. Our results in the PRP group can be compared with the study conducted by Wang-Saegusa et al.,[27] Filardo et al.[28] who reported an improvement in the outcome till six months which is similar to our study.

Rayegani et al.[29] investigated the effect of two IA injections of PRP administered at the 4-week interval on pain, stiffness, function, and quality of life in patients with OA knee and showed significant improvement (p value < 0.05) in WOMAC scores at six months after the treatment when compared with the baseline scores. The results in the group P of our study are similar to their research. No major complications like infection were noted. This agrees with other study reports and accredits the safety profile of autologous PRP IA injections.

PRP holds a promising solution in the management in OA knee in the present state of knowledge. Though PRP has consistently been shown to be superior to other intraarticular agents. There are many grey areas in the understanding of PRP and OA. Hence many more focused clinical studies are required. Further research is needed to determine the subset of patients which can benefit from PRP so that more individualized treatment strategies can be established.[4]

Limitations

The follow-up period in our study was only for six months. Long-term follow up is desirable. We lack objective evidence in the form of MRI of the knee or the measurement of cartilage thickness by ultrasonography in the assessment of the patients.

CONCLUSION

Intra-articular (IA) PRP is safe and more effective than steroids in alleviating pain in symptomatic OA knee. Improvement in the knee function was better with PRP than steroid group at short-term follow-up. To evaluate the long-term efficacy of PRP further research is required.

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