

COMPARISON OF PAIN RELIEF EFFICACY OF PLATELET-RICH PLASMA VERSUS CORTICOSTEROIDS IN KNEE OSTEOARTHRITIS

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ABSTRACT

Objective: To compare the pain relief efficacy of platelet rich plasma injection with corticosteroid injection in knee osteoarthritis using numeric rating scale.

Study Design: Quasi experimental study.

Place and Duration of Study: Department of Anesthesia and Pain Management, Combined Military Hospital Peshawar, from Jan 2018 to Dec 2019.

Methodology: Total of 310 patients who underwent knee injection for osteoarthritis were included in this study. Patients were divided into two groups; group A and group B comprising of 155 patients each. Patients in group 'A' received intra articular corticosteroid injection while patients in group 'B' received intra articular platelet rich plasma injection for knee osteoarthritis. Pain assessment via numerical rating score was done at the start of the treatment and at 6 months.

Results: In group A female to male ratio was 2.69:1 while in group B the female to male ratio was 2.78:1. Mean age of 'group A' was 58.52 ± 11.87 years and that of 'group B' was 58.79 ± 11.15 years. Numerical rating score pre-treatment in 'group A' vs 'group B' was 8.35 ± 1.17 vs 8.42 ± 1.14 . While numeric rating scale post treatment in 'group A' vs 'group B' was 5.74 ± 1.37 vs 4.06 ± 1.19 , respectively with *p*-value of 0.001, which is statistically significant.

Conclusion: Patients who received intra-articular platelet rich plasma had significantly more pain relief as compared to patients who received intra-articular steroid on numerical rating score.

Keywords: Corticosteroids, Injection, Intra-articular, Numerical rating score, Osteoarthritis knee, Platelet-rich plasma.

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INTRODUCTION

Osteoarthritis (OA) is a disease of joints especially bigger joints like knee. In this disease, the joint cartilage breaks down over time. This problem is among the five major causes of disability in adults. 3% of worldwide Years Lived Disability (YLD) is associated with osteoarthritis knee.¹ Knee Osteoarthritis (KOA) exhibits a strong female to male preponderance. Symptoms of knee osteoarthritis are not only limited to pain but also includes limitations on range of movements. This problem has a considerably negative impact on a person's lifestyle. As the average age has increased, the number of senior citizens is also growing, and along with obesity issues, it seems that the incidence of knee osteoarthritis has also risen.² Osteoarthritis results from an imbalance between inflammatory, anti-inflammatory cytokines and tumor necrosis factor-1, leading to the breakdown of cartilage.³

Treatment options for KOA includes non-pharmacological approaches like weight reduction, life style modifications and various physiotherapy

techniques. While pharmacologic therapies, including oral, topical, strontium ranelate, IL-1 receptor antagonist, antibodies nerve growth factors, intra articular corticosteroids and hyaluronic acid (HA) injections.⁴ The corticosteroid effects are mainly anti-inflammatory, mediated by inhibiting inflammatory cytokines like Interleukin 1a (IL-1a), Interleukin 1 (IL-1) and Tumor Necrosis Factor Alpha (TNF- α). Thus blocking the pathways leading to their destructive actions on joint cartilages.⁵ Corticosteroid joint injection has been used to treat OA for the last five decades and finds its recommended use in different guidelines, published by The American College of Rheumatology (ACR).⁶

These above-mentioned techniques mostly work as damage control strategies and sort of fire extinguishing efforts, not addressing the core issues of repair and regeneration of joint cartilage. Latest scientific work is focusing on the identification of biochemical pathways that can be specifically targeted therapeutically via biological intervention for repair of cartilage. Regenerative treatment modalities, such as the one with Platelet-Rich Plasma (PRP), have been studied in many researches. The growth factors in PRP can activate cartilage regeneration, pain reduction,

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improvement in joint mobility and resultantly the quality of life.⁷ Insulin-Like Growth Factor (IGF) stimulates cell proliferation, accelerating production of collagen, and causing the migration of fibroblasts. Multiple centered studies have indicated that PRP is superior in relieving pain of KOA patients as compared to steroids.^{8,9}

The objective assessment of pain after receiving intra articular injections can be easily assessed using Numerical Rating Score (NRS).¹⁰ The aim of our study was to compare pain relief using NRS scale in medium term duration using corticosteroid injection in KOA, with PRP joint injection. The results of this study will help in establishing the role of PRP in OA related joint pain for short-term duration to improve quality of life of these patients. PRP will not only help in reducing the suffering of osteoarthritic patients but will reverse the damage already done and will prevent further disease progression.

METHODOLOGY

This quasi experimental study were conducted at the department of Anesthesia and Pain Management, Combined Military Hospital Peshawar, from January 2018 to December 2019. World Health Organization (WHO) sample size calculator was used to calculate sample size of the study with 5% level of significance and 90% power of test. Anticipated population proportion 1 is 63.2% and anticipated population proportion 2-45.1%.⁵ Sample size came out to be 155 in each group and 310 in total. Lottery method sampling technique was employed.

Inclusion Criteria: Patients of both genders above 30 years of age, symptomatic knee joint for more than one year, pain NRS (NRS >6), Kellgren and Lawrence OA grade II, III, IV¹¹ and patient's willingness.

Exclusion Criteria: Patients with inability to understand and use NRS, patients with advanced rheumatoid arthritis or any other joint deformities, high uric acid levels, on antiplatelet drugs, previous knee surgeries and history of intra-articular injection within previous six weeks.

Patients in group 'A' received intra articular triamcinolone 40mg diluted with 4ml 0.9% normal saline (total 5ml) while patients in group 'B' received platelet rich plasma injection (total 5ml) for KOA.

In group A, 40 ml of blood was drawn from patients to make them blind to the study. Five ml of diluted 40 mg triamcinolone was injected in group A intra-articularly. While in group B, PRP was prepared

by obtaining 40ml of autologous blood. To prevent clotting 2ml of ACD-A (Anticoagulant Citrate Dextrose Solution, Solution A,) was introduced to the sample. Two centrifuge cycles were run. The first one was done at 1600 Relative Centrifugal Force (RCF) for 6 minutes to separate the erythrocytes and the second spin cycle was performed at 2000 RCF for 6 minutes to concentrate platelets, to produce 5 ml PRP. Activation of PRP solution was achieved by introduction of 0.5 ml of a calcium gluconate solution (1 g/10 ml). PRP prepared was graded as P2xB¹² as per Delong (PAW) classification. The solution was injected into each patient's knee immediately after preparation. Pain assessment via NRS was done at before the treatment and at six months after start of treatment. Details of the patient along with above-mentioned data were recorded on a preformed proforma. All patients were given due respect and their comfort was taken care of during the study. In both groups ultrasound guided intra-articular injections were given after taking strict aseptic measure.

Data were entered and analyzed using SPSS-20. Pain was measured using NRS scoring in both the groups. Chi-square test was calculated. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 310 patients receiving knee injection for osteoarthritis were included in this study. Patients were segregated into group A and group B comprising of 155 patients each. Mean age of study population was 58.43 ± 12.65 year. Out of study population, 83 (26.77%) were males and 227 (73.23%) were females. Group wise demographic data of patients are represented in Table-I. Difference in mean age and gender was not statistically significant between both the groups (*p*=0.322 and 0.629 respectively).

Table-I: Demographic comparison between the groups.

| Parameters | Group A (Corticosteroid) (n=155) | Group B (PRP) (n=155) | <i>p</i> -value |
|---------------|--|-----------------------------|-----------------|
| Age in Years | 58.52 ± 11.87 | 58.79 ± 11.15 | 0.322 |
| Gender | | | |
| Female | 113 (72.9%) | 114 (73.5%) | 0.629 |
| Male | 42 (27.1%) | 41 (26.5%) | |

Patients in both the groups were analyzed for OA as per Kellgren and Lawrence Osteo-arthritis grades on x-ray as per Table-II. NRS pre-treatment had a *p*-value of 0.998 compared to a *p*-value 0.001 post treatment which was significant (Table-III).

Table-II: Comparison between the groups with respect to Kellgren and Lawrence osteoarthritis grades.

| Kellgren and Lawrence Osteoarthritis Grades | Group A (corticosteroid) (n=155) | Group B (PRP) (n=155) | p-value |
|---|----------------------------------|-----------------------|---------|
| Grade-2 | 21 (13.5%) | 23 (14.8%) | 0.032 |
| Grade-3 | 81 (52.2%) | 78 (50.3%) | |
| Grade-4 | 53 (34.2%) | 54 (34.8%) | |

Table-III: Numeric rating scale (NRS) comparison between the study groups.

| Parameters | Group A (Corticosteroid) (n=155) | Group B (PRP) (n=155) | p-value |
|-------------------------------------|----------------------------------|-----------------------|---------|
| Pre-Treatment Numeric Rating Scale | 8.35 ± 1.17 | 8.42 ± 1.14 | 0.998 |
| Post-Treatment Numeric Rating Scale | 5.74 ± 1.37 | 4.06 ± 1.19 | 0.001 |

DISCUSSION

The fourth leading cause of YLD is osteoarthritis, accounting for 3% of total global YLD's.¹ KOA is more prevalent in females as compared to males. Symptoms of knee KOA are not limited to pain and also include physical limitations on range of movements. Osteoarthritis results from disturbances between inflammatory, anti-inflammatory cytokines and tumor necrosis factor-1. There are various treatment modalities for this disease. Pharmacological treatments include corticosteroids, and intra-articular hyaluronic acid (HA) injections.⁵ The results of corticosteroids are mediated by inhibiting inflammatory cytokines like IL-1 α , IL-1 and TNF- α thus blocking the pathways leading to their destructive actions of joint cartilages. PRP, HA and CS have been studied for their role in pain management associated with KOA and are being used in recent years to treat KOA.⁶ PRP, causes cartilage to regenerate resulting in pain reduction, increased joint mobility resulting in better quality of life.⁷

Therefore, in our study we compared pain relief in short-medium term duration with CS injection in KOA, which is conventional method, to PRP. Total of 310 patients underwent knee injection for osteoarthritis. Patients were placed into two groups comprising of 155 patients each. Those who were in group 'A' received triamcinolone 40mg injection while patients in group 'B' received intra articular PRP injection. NRS was compared between the two groups. NRS before treatment in 'group A' (corticosteroid) vs 'group B' (PRP) was 8.35 ± 1.17 vs 8.42 ± 1.14. NRS post treatment at 6 months in 'group A' vs 'group B' was 5.74 ±

1.37 vs 4.06 ± 1.19, respectively with p-value of 0.001, which is statistically significant.

The findings of our study were comparable with the study conducted by Forogh *et al.*⁵ In their study, a comparison of single dose of PRP injection with that of methylprednisolone acetate was made. The results of their study concluded that PRP treatment was superior for the patient's pain and symptom relief, improving quality of life and helped in performance of activities of daily living as compared to CS. This study showed that mean severity of pain in the group receiving CS before intervention was 79.1 ± 13.4. It changed to 63.2 ± 19.7 in second months and 72.5 ± 16.2, in sixth month follow-up. The severity of pain in the group treated with PRP was 80.4 ± 14.4 before intervention and turned into 45.1 ± 23.4 in the second month follow-up and 44.6 ± 15.6 in the sixth month follow-up. The treatment with PRP has significantly relieved the patients' pain in two and six months follow-up ($p < 0.001$). This is comparable to our study. Findings of our study were also comparable to Huang *et al.*⁶ Their study included 120 patients, who were randomized into 3 groups. The degree of improvement was significant in all groups as observed by all scores (WOMAC, NRS) in each group compared to the pretreatment values ($p < 0.05$). The mean WOMAC scores for the IA-HA group from before treatment to 3, 6, 9, and 12 months were 47.23 ± 5.37, 25.02 ± 4.98, 26.38 ± 5.20, 27.86 ± 4.34, and 30.64 ± 8.36, respectively. Comparable improvements were seen in the IA-CS and IA-PRP groups as well. There were no significant changes in the WOMAC scores between the 3 groups 3 months after treatment ($p > 0.05$) but IA-PRP showed a considerably lower score 6, 9 and 12 months after treatment ($p < 0.05$). PRP injection into the knee for symptomatic early stages of KOA is a valid treatment option. The clinical efficacy of IA PRP is comparable to that of the IA-HA and IA CS forms after 3 months and the long-term efficacy of IA PRP is superior to IA-HA and IA-CS.

Several other studies compared the effects of IA-CS (CS) with PRP in KOA. Barac *et al.*⁷ in his study included 53 patients (90 knees). They followed these patients up to 12 months after the last injection. Patient follow up was scheduled at 2, 6 and 12 months after the last IA injection. The different pain scores (NRS, WOMAC, IKDC and KOOS) for the Cellular Matrix (CM) Group were documented at 2, 6 and 12 months after the last injection. After a gap of two months after the last injection, there were statistically significant differences in CM group when compared to sodium

hyaluronate (ArthroVisc®, AV) and sodium hyaluronate with mannitol (Ostenil® Plus, OP) OP groups in NRS, WOMAC, KOOS and IKDC scores with $p < 0.05$. In patients treated with CM-PR-PHA, there was statistically significant ($p < 0.05$) improvement in cartilage thickness already after 2 months and also after 6 and 12 months in medial compartment, and high statistically significant improvement ($p < 0.001$) in lateral compartments.

Meheux *et al.*¹³ examined patients with painful KOA, and concluded that PRP showed remarkable clinical improvements up to 12 months post injection. Clinical outcomes and WOMAC scores were also considerably better after PRP as compared to HA at 3-12 months post injection. However, there is low evidence for comparing leukocyte-rich versus leukocyte-poor PRP or PRP versus steroids in this study as they provided level I significance.

Finally, results of almost majority of the studies conducted in different populations of the world in comparing pain relief with CS injection versus PRP injection in KOA have shown promising results in favor of PRP.¹⁴⁻¹⁶ They all agree on the basis that CS injections mostly work as damage control strategy, not addresses the core issues of repair and regeneration of joint cartilage. Current research is now focusing, to pin point main pathways that can be chosen therapeutically via biological intervention for repair and regeneration of cartilage. Currently available regenerative, minimally invasive therapies, like PRP, have been researched in a number of these studies. PRP, with its growth factors triggers cartilage regeneration that results in reduction of pain, improved functionality of the joint and hence the quality of life. Alpha granules deliver a vast amount of growth factors from enriched platelets, such as, PDG (Plated Derived Growth Factor) which result in growth of cells, regeneration and repair of blood vessels, along with collagen production, TGF beta (Transforming Growth Factor Beta) enhances cell proliferation, and production of extracellular matrix, causing angiogenesis and resultantly healing wound healing, VEGF (Vascular Endothelial Growth Factor) causes cell division and movement of endothelial cells, FGF (Fibroblast Growth Factor) which causes proliferation, EGF (Epidermal Growth Factor) effects angiogenesis, controls changes of the extracellular matrix (ECM), and hence division and migration of fibroblasts, IGF (Insulin like Growth Factor) which stimulates cell division, speeds up production of collagen, and stimulates the movement of fibroblasts.^{17,18} By

comparing both methods in short to medium term, duration i.e. at 2-3 months helped us to choose a PRP is a better method in not only relieving the osteoarthritis pain but also regenerating and repairing the damage done due to disease process. Here we finally recommend that PRP injection not only reduced the suffering of osteoarthritic patients but will reverse the damage already done and thus prevented further disease progression.

CONCLUSION

Patients who received intra-articular platelet rich plasma had significant more pain relief as compared to patients who received intra-articular steroid on numerical rating score.

LIMITATION OF STUDY

This study only measured a pain score on NRS and that too at 6 months duration. This limitation was most profound in shorter duration and not taking into account a further elaborate functional score like WOMAC along with some radiological modalities. This study was conducted in a limited set up in Peshawar and surrounding population so its results might not be a true representation of national or international population.

Conflict of Interest: None.

Authors' Contribution

AS: Writing original draft, AYZ: Data collection, data analysis, SHF: Data collection, data analysis, MS: Article drafting, SKN: Article drafting, MS: Literature research.

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