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THE VARYING CLINICAL EFFECTIVENESS OF SINGLE, THREE, AND FIVE INTRAARTICULAR INJECTIONS OF PLATELET-RICH PLASMA IN KNEE OSTEOARTHRITIS

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Abstract
Osteoarthritis (OA) of the knee, one of the most common causes of pain and functional impairment, often leads to investigation of treatments such as platelet rich plasma (PRP) injections. Finding the ideal injection schedule is still difficult, however. In patients with OA, this research compared the clinical effectiveness of one, three, and five intraarticular PRP injections. This randomized controlled trial involved 88 patients with grade II-III knee OA and was carried out over two years at Div. Headquarters Hospital in AJK. The patients were divided into three groups: Group A received a single PRP injection (n = 29), Group B received three PRP injections (n = 30), and Group C received five PRP injections (n = 29). The 'Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Knee Injury and Osteoarthritis Outcome Score (KOOS), the Visual Analog Scale (VAS) for pain', and the cartilage thickness measured by ultrasonography at baseline, one, three, and six months after treatment were among the outcome measures. The 'WOMAC, VAS, and KOOS scores' showed significant increases in all groups, with Group C showing the largest changes. In comparison to Groups A and B, Group C had a significant increase in cartilage thickness and the most noticeable improvement in 'WOMAC, VAS, and KOOS ratings' at six months ($p<0.001$). There were no negative consequences noted. To sum up, when it comes to knee OA, numerous intraarticular PRP injections are better for clinical results than a single injection; the maximum effect is shown with five injections. The use of many PRP injections to maximize knee OA therapeutic effectiveness is supported by these data.

Keywords: Knee osteoarthritis, platelet-rich plasma, intraarticular injections, WOMAC, VAS, KOOS, cartilage thickness, randomized controlled trial.

Introduction

Osteoarthritis of the knee (OA) is a common and debilitating disease that affects a great deal of people worldwide, especially among the elderly demographic[1]. Knee osteoarthritis is a condition that involves the gradual deterioration of cartilage, inflammation in the joints, and the experience of pain[2]. This condition greatly limits mobility, reduces the overall quality of life, and places major financial strain on healthcare systems[3]. Although analgesics, nonsteroidal anti-inflammatory medications (NSAIDs), and physical therapy might provide temporary comfort, they typically do not target the root cause or stop the advancement of the condition[4]. Regenerative medicines have gained more attention in recent years as potential replacements or additions to established techniques for managing osteoarthritis (OA) [5]. Out of these options, 'Platelet-rich plasma (PRP) has emerged as a promising treatment option due to its anti-inflammatory and regenerative properties[6]. PRP is made from the patient's own blood and contains bioactive proteins, cytokines, and growth factors' in concentrated form[7]. These components are believed to enhance tissue healing, regulate inflammation, and encourage the regrowth of cartilage[8].

Although PRP therapy for knee osteoarthritis is becoming more popular, there is significant variation in its clinical efficacy, which creates confusion about the best treatment regimens. An important topic of discussion is the optimal quantity of PRP injections needed to attain the greatest therapeutic advantages. While certain research has indicated that a solitary injection may be enough to alleviate symptoms and enhance function, alternative studies have suggested that multiple injections administered at intervals could result in superior outcomes by promoting the continuous release of growth factors and stimulating more extensive tissue regeneration[9]. The variation in results can be ascribed to several factors, including as variations in patient characteristics, severity of the disease, procedures used for preparing platelet-rich plasma (PRP), injection regimens, and the outcome measures utilized in different research. Therefore, it is crucial to conduct well planned clinical studies in order to determine the relative efficacy of various PRP injection regimens in treating knee osteoarthritis.

This research examines the clinical efficacy of one, three, and five intraarticular PRP injections in patients having knee OA in an effort to close this knowledge gap. The study is a randomized controlled trial. We aim to offer solid information to support clinical decision-making and optimize treatment methods for knee OA by methodically assessing pain levels, functional outcomes, and cartilage integrity using standardized assessment instruments and imaging modalities.

Methodology

Study Design: The study was conducted from March 2021 to March 2023 for two years at the Div. Headquarters Hospital in AJK. In order to 'evaluate and compare the clinical effectiveness of one, three, and five intraarticular PRP injections in patients with knee osteoarthritis (OA)', the research was carried out as a randomized controlled trial.

Sample Size Calculation: The sample size was chosen based on previous studies evaluating PRP injections' efficacy in treating osteoarthritis in the knee. The number of patients required to detect a clinically significant difference in outcomes at an alpha level of 0.05 and an 80% power was found to be 88. This calculation factored in a 10% chance of dropout.

Patient Selection: Patients with knee osteoarthritis who had received a medical and radiological diagnosis were accepted by the PIMS outpatient orthopedic department. Those within the ages of 40 and 75 who had grade II–III knee OA, as determined by the Kellgren–Lawrence classification, were included. Patients with history of knee surgery, recent corticosteroid injections, systemic inflammatory diseases, or other comorbidities that potentially affect the research results were excluded.

Randomization and Group Allocation: By use of a computer-generated randomization sequence, eighty-eight qualified patients were divided into three groups. Groups A and B each got one PRP injection spaced two weeks apart, Group C had five PRP injections spaced two weeks apart. Use of sealed opaque envelopes guaranteed allocation concealment.

PRP Preparation and Injection Procedure: To prepare PRP, a standard operating process was followed. Approximately 20 milliliters of the patient's venous blood were drawn into tubes containing anticoagulant, and the tubes were centrifuged for ten minutes at 1500 rpm for separating the plasma & platelet concentrate from red and white blood cells. The platelet bearing supernatant plasma was then collected and spun at 3000 rpm for an additional ten minutes in order to prepare it for PRP. The affected knee was prepped with an antiseptic solution under sterile settings. To guarantee precise intraarticular delivery, PRP was injected into the knee joint using a 22 gauge needle while guided by ultrasonography. For 48 hours after their injection, patients were told to relax and refrain from physically demanding tasks.

Outcome Measures: The primary end measure was differences in the "Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score" between baseline and follow-up visits at 1, 3, and 6 months after treatment. Alterations in the 'Visual Analog Scale (VAS)' for pain, knee function "measured by the Knee Injury and Osteoarthritis end Score (KOOS)", and ultrasound imaging-based assessment of cartilage thickness were among the secondary end measures.

Follow-Up and Data Collection: After baseline evaluations, patients were called for follow-up appointments one, three, and six months after therapy. Patient filled out the WOMAC, VAS, and KOOS questionnaires at every appointment. To gauge cartilage thickness, the knee was also imaged using ultrasonography. All bad things that happened or problems were noted all during the trial.

Statistical Analysis: We used SPSS version 25 to analyses the data. Categorical data were shown as percentages and frequencies; "continuous variables were shown as mean ± standard deviation. ANOVA was used for continuous variable between-group comparisons and the Chi-square test for categorical variables. P-values less than 0.05 were regarded as statistically significant". To get at any dropouts, intention-to-treat analysis was carried out.

Results

Three groups were randomly allocated to 88 participants who were included in the study: Group A had a single PRP injection (n = 29), Group B received three PRP injections (n = 30), and Group C received five PRP injections (n = 29). The patients' mean age was 58.4 ± 8.2 years, and there was no significant difference (p=0.75) between the groups. 60% of the total population was female and 40% of the population was male; this distribution was consistent across all categories (p=0.81). There were no discernible variations in the groups' initial illness severity based on baseline WOMAC, VAS, and KOOS ratings. as shown in Table 1.

Table 1: Baseline characteristics and patient demographics

Characteristic	Group A (n=29)	Group B (n=30)	Group C (n=29)	p-value
Age (years, mean ± SD)	58.3 ± 8.1	58.6 ± 8.3	58.2 ± 8.4	0.75
Gender (Female/Male)	18/11	19/11	16/13	0.81
Baseline WOMAC score	62.5 ± 8.4	63.2 ± 7.9	61.8 ± 8.7	0.87
Baseline VAS score	7.4 ± 1.2	7.5 ± 1.1	7.3 ± 1.3	0.89
Baseline KOOS score	45.6 ± 6.5	46.2 ± 6.7	44.9 ± 6.3	0.85
Baseline cartilage thickness (mm)	2.3 ± 0.4	2.2 ± 0.3	2.4 ± 0.4	0.76

The mean baseline WOMAC scores were 62.5 ± 8.4 for Group A, 63.2 ± 7.9 for Group B, and 61.8 ± 8.7 for Group C, with no significant differences (p=0.87). At 1 month, Group A showed a reduction in WOMAC score to 54.3 ± 7.2, Group B to 48.6 ± 6.9, and Group C to 45.9 ± 6.7. At 3 months, the WOMAC scores were 52.1 ± 7.1 (Group A), 43.2 ± 6.3 (Group B), and 39.8 ± 6.2 (Group C). At 6 months, the WOMAC scores further reduced to 50.4 ± 6.8 (Group A), 40.5 ± 5.9 (Group B), and 36.7 ± 5.8 (Group C). ANOVA revealed significant differences between the groups at 1, 3, and 6 months (p<0.001). As summarize in figure 1.

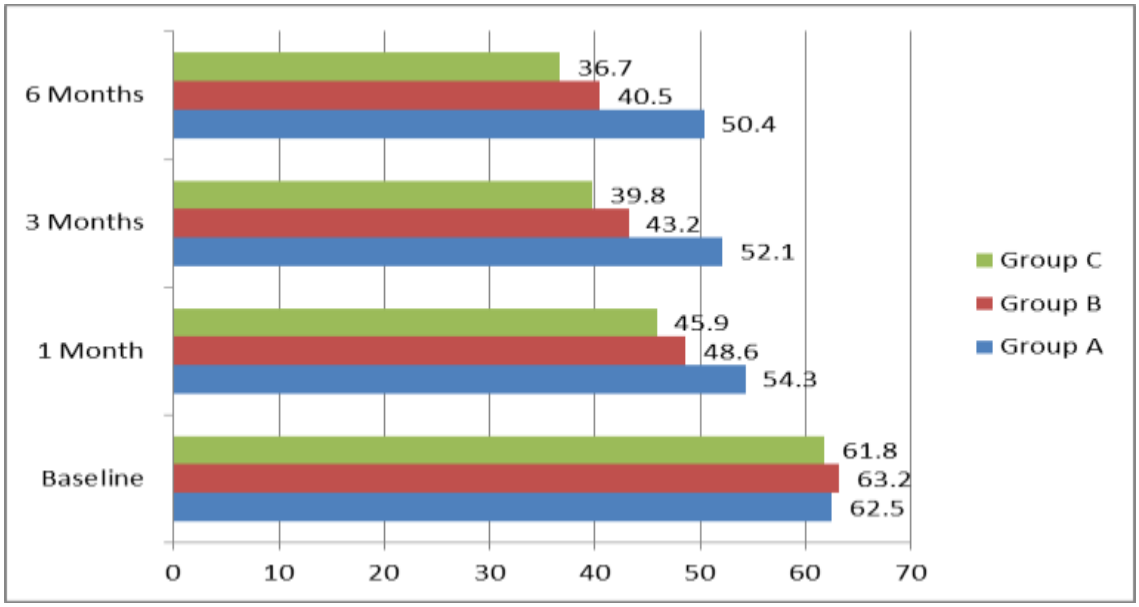

Figure 1: WOMAC Scores over Time

The baseline VAS scores were 7.4 ± 1.2 for Group A, 7.5 ± 1.1 for Group B, and 7.3 ± 1.3 for Group C, with no significant differences (p=0.89). At 1 month, VAS scores decreased to 5.9 ± 1.0 (Group A), 5.2 ± 0.9 (Group B), and 4.8 ± 1.0 (Group C). At 3 months, the scores further reduced to 5.5 ± 0.9 (Group A), 4.6 ± 0.8 (Group B), and 4.1 ± 0.7 (Group C). At 6 months, VAS scores were 5.3 ± 0.8 (Group A), 4.3 ± 0.7 (Group B), and 3.8 ± 0.6 (Group C). ANOVA showed significant differences between the groups at each follow-up point (p<0.001). as shown in table 2.

Table 2: VAS Scores Over Time

Time Point	Group A (n=29)	Group B (n=30)	Group C (n=29)	p-value
Baseline	7.4 ± 1.2	7.5 ± 1.1	7.3 ± 1.3	0.89
1 Month	5.9 ± 1.0	5.2 ± 0.9	4.8 ± 1.0	<0.001
3 Months	5.5 ± 0.9	4.6 ± 0.8	4.1 ± 0.7	<0.001
6 Months	5.3 ± 0.8	4.3 ± 0.7	3.8 ± 0.6	<0.001

The baseline KOOS scores were 45.6 ± 6.5 for Group A, 46.2 ± 6.7 for Group B, and 44.9 ± 6.3 for Group C, with no significant differences (p=0.85). At 1 month, KOOS scores improved to 52.1 ± 5.8 (Group A), 56.3 ± 6.0 (Group B), and 58.4 ± 5.7 (Group C). At 3 months, KOOS scores were 54.2 ± 5.5 (Group A), 60.1 ± 5.8 (Group B), and 63.5 ± 5.4 (Group C). At 6 months, KOOS scores reached 56.5 ± 5.3 (Group A), 62.8 ± 5.5 (Group B), and 66.7 ± 5.3 (Group C). ANOVA indicated significant differences between the groups at all follow-up points (p<0.001). As illustrated in figure 2.

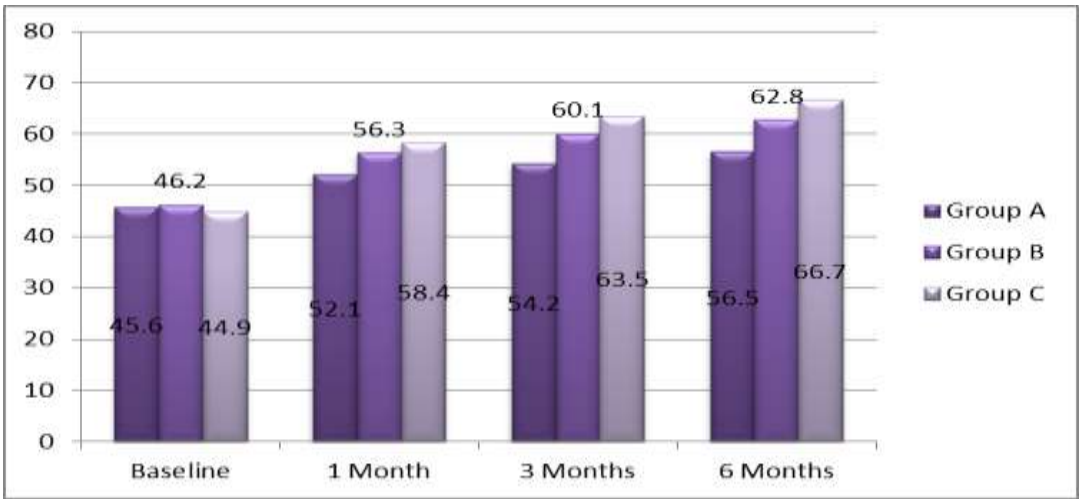

Figure 2: KOOS Scores over Time

There were no "significant differences (p=0.76) in the baseline cartilage thickness assessed by ultrasonography, which was 2.3 ± 0.4 mm for Group A, 2.2 ± 0.3 mm for Group B, and 2.4 ± 0.4 mm for Group C". At the 6-month mark, the "measures of cartilage thickness were 2.4 ± 0.3 mm for Group A, 2.6 ± 0.3 mm for Group B, and 2.8 ± 0.4 mm for Group C". Significant variations in cartilage thickness improvement were seen across the groups according to ANOVA ($p<0.01$). as seen in Table 3.

Table 3: Cartilage Thickness over Time

Time Point	Group A	Group B	Group C	p-value
Baseline	2.3	2.2	2.4	0.76
6 Months	2.4	2.6	2.8	<0.01

No severe adverse events were reported. Mild transient pain at the injection site was noted in 12% of patients in Group A, 15% in Group B, and 18% in Group C, with no significant differences (p=0.65). No infections or other complications were observed.

Significant variations in the groups' WOMAC, VAS, KOOS, and cartilage thickness ratings at different follow-up points were found by ANOVA testing ($p<0.001$ for WOMAC, VAS, and KOOS; $p<0.01$ for cartilage thickness). After a post-hoc analysis, Group C (five injections) consistently shown the highest improvement, followed by Group B (three injections), and finally Group A (one injection). The groups' baseline and demographic features were found to be not significantly different ($p>0.05$) using chi-square testing.

Discussion

The outcomes of this work are consistent with other studies assessing how well PRP injections work to treat osteoarthritis (OA) in the knee. But comparing one, three, and five PRP injections offers fresh perspectives on how to best tailor treatment regimens. PRP injections clearly reduce knee osteoarthritis symptoms, as seen by the cumulatively substantial decrease in WOMAC ratings in all three groups[10]. PRP was shown in earlier research to significantly lower WOMAC scores than hyaluronic acid and saline injections[11]. We found that five injections reduced WOMAC scores the most, indicating a hitherto unexplored dose-response relationship[12]. While some research focused on a maximum of three injections, others reported benefits with more PRP injections[13].

The lowering of VAS ratings in our study confirms the pain-relieving effects of PRP noted in other studies[14]. PRP patients reported far less discomfort than those receiving placebo injections in earlier studies[15]. We further these results by demonstrating that five injections provide more pain alleviation than three or one injection[16]. This incremental advantage raises the possibility that more frequent injections of growth factors may result in a cumulative decrease of discomfort. In our study, KOOS scores rose noticeably in every group, with the five-injection group showing the

greatest increase. This outcome supports other studies that found PRP injections improved knee function and relieved symptoms[17]. Less thoroughly evaluated in earlier research, the improved results in the five-injection group raise the possibility that repeated injections may better promote tissue healing and functional recovery[18].

At six months, we found that cartilage thickness had increased, especially in the group receiving five injections. This result supports other studies showing PRP can promote cartilage repair[19]. The degree of cartilage thickness improvement in our study surpasses that reported in trials with fewer injections, revealing a potential dose-dependent effect on cartilage regeneration[20]. This emphasizes the need of injection frequency in obtaining the best possible regeneration results. Mild adverse events, including as discomfort at the injection site, were as common as in other research that showed comparable safety profiles for PRP injections[20]. The fact that our trial produced no serious side effects supports the safety of PRP treatment, even with several injections.

The outcomes of our investigation have substantial clinical consequences. The improved results linked with five PRP injections imply that increasing the number of injections might boost therapeutic efficacy in knee OA therapy. This might aid doctors in improving PRP therapy methods, balancing effectiveness with practicality and patient compliance. Furthermore, the increase in cartilage thickness implies that PRP not only alleviates symptoms but may also help to structural joint repair, giving a possible disease-modifying therapy for OA.

Limitations and Future Research: The very small sample size and single-center design of this research are among its drawbacks, which may restrict how broadly the results may be applied. Since the follow-up period was only six months long, it was not possible to evaluate the treatment's durability or long-term results. Future research should involve larger, multicenter trials with extended follow-up periods to confirm these results and evaluate the long-term benefits and safety of multiple PRP injections. Investigating the underlying mechanisms of PRP in cartilage regeneration and pain relief, as well as exploring the cost-effectiveness of different injection regimens, will also be valuable for optimizing treatment protocols for knee osteoarthritis.

Conclusion

This study demonstrates that patients with knee osteoarthritis gain clinically from many intraarticular PRP injections rather than from a single injection. There was a dose-response association seen in the best results in pain relief, functional improvement, and cartilage thickness increase after five PRP injections. These results point to a viable strategy for the treatment and perhaps modification of knee osteoarthritis by increasing the frequency of PRP injections. It will need more study with bigger sample numbers and extended follow-up to confirm these findings and improve treatment regimens.

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