

Original research article

The efficacy and functional outcome of intra-articular infiltration of autologous platelet rich plasma in early osteoarthritis knee

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Abstract

Most of the treatments for osteoarthritis at recent times are palliative and mainly treat the symptoms rather than influencing the biochemical environment of the joint. Meanwhile, autologous platelet-rich plasma has emerged as a treatment option for tendinopathies and chronic wounds. After obtaining clearance and approval from the institutional ethical committee and patients fulfilling the inclusion criteria were considered for the study after obtaining informed consent. The demographic data and relevant history of the study participants were collected, and necessary clinical and radiological examination was performed. The mean VAS score of the study participants at the baseline was 6.54 with a standard deviation of around ± 0.719 . This implies that the study participants were experiencing more pain before the intervention. Later, the follow up was made on 3 different occasions. The variation in VAS scores from the baseline was compared in each follow up i.e., 6 weeks, 3 months, and 6 months after the intervention. In the study, the mean WOMAC score of the participants at the baseline was 71.07 with a standard deviation of around ± 3.826 . This implies that the study participants were experiencing more pain, increased stiffness, and disturbed function of the joint before the intervention. Later, the follow up was made on 3 different occasions. The variation in WOMAC scores from the baseline was compared in each follow up i.e., 6 weeks, 3 months, and 6 months after the intervention.

Keywords: Intra-articular infiltration, autologous platelet rich plasma, early osteoarthritis knee

Introduction

Osteoarthritis (OA) of the knee joint has been considered as one of the leading cause of musculoskeletal disability. It is clinically heterogeneous, and results in structural and functional failure of synovial joints. It is characterized by progressive destruction of joint cartilage, sclerosis of sub-chondral bone, changes in the synovial membrane and reduced viscosity of the synovial fluid ^[1]. Major leading risk factors for development of osteoarthritis are age, genetics and obesity ^[2]. As a result of increased lifespan and obesity, the prevalence of osteoarthritis is on the rise in Indian population accounting around 22% to 39% ^[3].

Earlier, joint overloading and mechanical stress was thought to be the main risk factor contributing to etiopathogenesis of OA. However, in the last couple of decades, growing emphasis has been directed towards biomechanical factors that are required for maintenance of cartilage health. In recent scenario, imbalance in biochemical factor has been stressed upon. This imbalance can be addressed by targeting the biochemical elements that inhibit metalloproteases (IL-4, IL-10, IL-13, tissue inhibitor of metalloproteinases, insulin-like growth factor (IGF), and transforming growth factor-b) and the biochemical elements that enhance their synthesis (IL-1b, tumor necrosis factor-a, IL-8, IL-6, IL-17, IL-18, leukemia inhibitory factor, and nitric oxide) ^[4].

Options for the management of OA knee are limited and the available non-surgical options provide symptomatic relief that too for a short duration of time. No disease modifying therapies that can alter the course of disease are available till date and this leads to patients inclining more towards invasive procedures for alleviation of pain ^[5]. However, non-operative methods are the mainstay of treatment of early osteoarthritis knee.

Best among such proposed methods is Platelet Rich Plasma (PRP), which is by definition, a volume of the plasma fraction of autologous blood having a platelet concentration above baseline ^[6]. Several studies

have suggested that a three to four fold increase in the baseline platelet concentration should be achieved [7]. PRP injections have been reported to be more effective than corticosteroid injections in relieving pain and improving function in early osteoarthritis knee [8]. Alpha granules of platelets in PRP contains cytokines like PDGF, TGF- beta, IGF, FGF, VEGF, EGF, which enhances tissue regeneration and healing, and help in removal of degenerated and necrotic tissue [9].

Moreover, most of the treatments for osteoarthritis at recent times are palliative and mainly treat the symptoms rather than influencing the biochemical environment of the joint. Meanwhile, autologous platelet-rich plasma has emerged as a treatment option for tendinopathies and chronic wounds. In addition to release of growth factors, platelet-rich plasma also promotes concentrated anti-inflammatory signals including interleukin-1a, which has been a focus of emerging treatments for osteoarthritis [10]. The purpose of this study was to investigate whether platelet rich plasma infiltration in symptomatic early knee osteoarthritis is associated with good clinical outcomes.

Methodology

Type of the Study: Prospective clinical study

Sample Size: The sample study of our study was 55

Inclusion Criteria

- Age more than 40 years of either genders
- Patients who give informed consent and willing for follow up
- Patients with osteoarthritis knee of grade ≤ 2 as per Kellgren-Lawrence scale

Exclusion Criteria

- Age group less than 40 years
- Rheumatoid arthritis of knee joints
- Hematological diseases (coagulopathies)
- Active infections
- Patients with immunosuppression
- Patients on therapy with anticoagulants.

Method of data collection

After obtaining clearance and approval from the institutional ethical committee and patients fulfilling the inclusion criteria were considered for the study after obtaining informed consent. The demographic data and relevant history of the study participants were collected, and necessary clinical and radiological examination was performed.

- Demographic data and relevant history
- Clinical examination
- Investigations

Routine

- CBC with ESR, Random blood sugar and C-Reactive Protein
- Blood grouping and Cross matching
- Bleeding time and Clotting time
- Blood Urea, Serum Creatinine, RA factor, Serum Uric acid

Special: X-ray: Knee Joint (AP and Lateral Position)

Procedure

20 ml of blood will be taken from the cubital vein of the patient in a centrifuge vial which is preloaded with anticoagulant sodium citrate. The blood will be prepared and centrifuged at 1500 rpm for 15 min, following which the plasma will be separated. The plasma will again be centrifuged at 2500 rpm for 10 min to yield 3-4ml of PRP, following which 3-4 ml of PRP (Activated with calcium chloride), at the site of maximum tenderness and in the vicinity, with the patients knee in 45-90 degree flexion so that joint is opened for injection through lateral parapatellar approach. Under aseptic precaution 4 ml platelet concentrate was injected into knee joint using 20 gauge needle without local anesthetic.

Results

Table 1: Distribution of study participants based on laterality of the joint

Knee Involvement	Frequency (N)	Percentage (%)
Bilateral	23	41.8
Right	20	36.4
Left	12	21.8

Total	55	100.0%
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In the study, osteoarthritis of knee joint was affected on both sides in majority of the cases i.e., about 41.8%. The next common presentation was in right side, followed by left side laterality.

Table 2: Comparison of VAS over the follow up

Visual Analogue Scale		Mean	Standard Deviation	t-value	p-value
First Follow-Up	Baseline	6.54	0.719	16.279	<0.001
	6 weeks	5.70	0.838		
Second Follow-Up	Baseline	6.54	0.719	43.756	<0.001
	3 months	4.65	0.781		
Third Follow-Up	Baseline	6.54	0.719	73.022	<0.001
	6 months	3.63	0.808		

The mean VAS score of the study participants at the baseline was 6.54 with a standard deviation of around ± 0.719 . This implies that the study participants were experiencing more pain before the intervention. Later, the follow up was made on 3 different occasions. The variation in VAS scores from the baseline was compared in each follow up i.e., 6 weeks, 3 months, and 6 months after the intervention. On analysing the variation in means using paired sample t-test, the study found statistically significant relation in all 3 follow-ups, thereby suggesting that there was a lot of improvement in the condition of the participants as the mean values of VAS score decreased drastically.

Table 3: Comparison of WOMAC Score over the follow up

WOMAC Score		Mean	Standard Deviation	t-value	p-value
First Follow-Up	Baseline	71.07	3.826	46.071	<0.001
	6 weeks	66.24	3.986		
Second Follow-Up	Baseline	71.07	3.826	65.099	<0.001
	3 months	61.54	4.364		
Third Follow-Up	Baseline	71.07	3.826	87.012	<0.001
	6 months	56.28	4.393		

In the study, the mean WOMAC score of the participants at the baseline was 71.07 with a standard deviation of around ± 3.826 . This implies that the study participants were experiencing more pain, increased stiffness, and disturbed function of the joint before the intervention. Later, the follow up was made on 3 different occasions. The variation in WOMAC scores from the baseline was compared in each follow up i.e., 6 weeks, 3 months, and 6 months after the intervention. On analysing the variation in means using paired sample t-test, the study found statistically significant relation in all 3 follow-ups, thereby suggesting that there was a lot of improvement in the condition of the participants as the mean values of WOMAC score decreased drastically.

Table 4: Platelet concentration of the study participants

Platelet Concentration	Mean	Standard Deviation	Minimum	Maximum
Before the spin (In lakhs)	2.79	0.925	1.60	4.35
After 2nd spin (In lakhs)	13.17	4.795	4.80	27.95
Times increased	4.76	1.057	2.60	7.80

The platelet concentration was in the normal range in all the study participants i.e., between 1.5 to 4.5 lakh platelets per microliter of blood. The mean value of the platelet concentration before the spin was 2.79 lakh/ μ L with a standard deviation of around ± 0.925 lakh/ μ L. After spinning the platelet sample twice, the platelet concentration increased at an average of 4.76 times leading to the mean value of about 13.17 lakh/ μ L of platelet concentration in the sample collected from the study participants.

Discussion

Osteoarthritis of knee joint was affected on both sides in the present study in majority of the cases i.e., about 41.8%. The next common presentation was in right side, followed by left side laterality. This is completely similar to the study by Huang PH *et al.* [11] where the cases were presented as bilateral in majority. And the next common presentation was right sided. Moreover, few of the previous studies such as Filardo G *et al.* [12] and Patel S *et al.* [13] included exclusively the participants with bilateral involvement.

The platelet concentration was estimated in the study, and found to be in the normal range in all the participants i.e., between 1.5 to 4.5 lakh platelets per microliter of blood. The mean value before the spin was 2.79 lakh/ μ L with a standard deviation of around ± 0.925 lakh/ μ L. After spinning the platelet sample twice, the platelet concentration increased at an average of 4.76 times leading to the mean value of about

13.17 lakh/ μ L of platelet concentration in the sample collected from the study participants. This resembles the findings of the studies such as Huang PH *et al.* [11] and Raeissadat SA *et al.* [14], where the dual spin system was used to obtain the PRP. However, few studies such as Cole BJ *et al.* [15] and Halpern B *et al.* [16], had utilized the PRP as an intervention after single spin.

Visual Analogue Scale had been regarded as the best tool in appreciating the severity of the pain since decades. Thus, VAS was assessed in the present study, and the mean score of the participants at the baseline was estimated to be 6.54 with a standard deviation of around ± 0.719 . This implies that the study participants were experiencing more pain before the intervention. Later, the variation in VAS scores from the baseline was compared in each follow up i.e., 6 weeks, 3 months, and 6 months after the intervention. On analysing the variation in means using paired sample t-test, the study found statistically significant relation in all 3 follow-ups, thereby suggesting that there was a lot of improvement in the condition of the participants as the mean values of VAS score decreased drastically. This sort of improvement was seen in the studies by Buchard *et al.* [17], where the mean difference in VAS score from the baseline over the follow up period was around 3.58, which was statistically proven to be significant. In the study by Cole BJ *et al.* [15], the VAS score was lesser in the PRP group over the follow-up period in comparison with the Hyaluronic acid group. Even the study by Lana *et al.* observed similar findings. The timeline of observing VAS varied in different studies. The timeline of the present study completely mimics the study by Patel S *et al.* [13] where the parameters were recorded before the intervention, and at 6 weeks, 3 months and 6 months after the intervention. In case of Halpern B *et al.* [16] VAS was recorded at the start of the study followed by 6 and 12 months duration after the intervention. Whereas Forogh B *et al.* and Raeissadat SA *et al.* [14] observed the severity of pain at the beginning, and 2 and 6 months later. The study by Huang PH *et al.* [11] had the most follow-up measurements with the observations in the beginning, and at 1, 3, 6, 9, and 12 months' durations. Moreover one important aspect which should be mentioned is that VAS score reduced gradually over the follow-up period in all these studies confirming the efficacy of PRP in improving the condition of the patients.

In the present study, Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire was used to evaluate the outcome. Accordingly, the mean WOMAC score of the participants at the baseline was 71.07 with a standard deviation of around ± 3.826 . This implies that the study participants were experiencing more pain, increased stiffness, and disturbed function of the joint before the intervention. Also, this is quite huge compared to the previous studies such as Raeissadat SA *et al.* [14], Huang PH *et al.* [11], and Halpern B *et al.* [16] where the mean WOMAC total was around 30. Later, the variation in WOMAC scores from the baseline was compared in each follow up of the study i.e., 6 weeks, 3 months, and 6 months after the intervention. On analysing the variation in means using paired sample t-test, the study found statistically significant relation in all 3 follow-ups, thereby suggesting that there was a lot of improvement in the condition of the participants as the mean values of WOMAC score decreased drastically. This resembles the findings from the study by Halpern *et al.* [16], Cole BJ *et al.* [15], and Raeissadat *et al.* [14], where the WOMAC scores reduced significantly over the period of follow up [18].

Conclusion

On injecting the intra-articular infiltration of autologous platelet rich plasma in the patients with early osteoarthritis knee, the study observed the following;

- There was significant reduction in the pain over the joint of the participants as the mean values of VAS score decreased drastically
- Also the mean values of WOMAC score decreased gradually, thereby implying a lot of improvement in the condition of the participants

As the side effects post intervention were insignificant, the usage of intra-articular infiltration of platelet rich plasma in early osteoarthritis knee was proven to be safe.

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