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A study on the outcome of platelet-rich plasma in the management of primary osteoarthritis of knee in Northern Andhra Pradesh

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Abstract
Introduction: The present management line of osteoarthritis of the knee is mostly symptomatic, therefore the need to investigate treatment modality which addresses the disease process in itself. This study was undertaken to evaluate the efficacy of platelet-rich plasma in primary osteoarthritis of the knee.
Materials and Methods: This prospective study was done on 62 knees in 50 patients of early primary osteoarthritis of the knee. Three injections of platelet-rich plasma were given at four weeks interval and the outcome was evaluated using WOMAC and VAS score at pre-injection, 3 weeks, 12 weeks, and 24 weeks. Ahlback's grading was done at pre-injection and 6 months.
Results: Most of the cases in our series were in the age group of 51-60 years with female predominance, 38 cases had grade 2 disease and the remaining had grade 1 involvement. Improvement in WOMAC score parameters started at 3 weeks with progressive improvement at subsequent follow-ups. WOMAC score parameters (pain, stiffness, physical function, and total score) at pre-injection were 15.28, 6.16, 38.46, and 58.68 and at 6 months follow up were 6.02, 2.01, 18.46 and 26.51 respectively. A similar improvement was seen in the VAS score with a pre-injection score of 6.48 and a final score of 3.56. The average WOMAC score was less for grade 1 as compared to grade 2. Improvement was seen in most cases though the level varied from good to mild improvement. There was no complication related to the treatment in our series.
Conclusion: It is evident from the study that PRP is an effective modality of treatment. However, further high evidence studies are required to look for the long-term effects and to confirm the findings of this study.

Keywords: Platelet-rich plasma, osteoarthritis, intraarticular injection, PRP in the knee.

Introduction
Osteoarthritis (OA) is the most predominant form of arthritis and the main cause of disability in the people aged 65 and older [1]. It is a clinically varied and poorly understood disease. Although most research has looked at the destruction of the cartilage, arthritis is often now considered in terms of organ failure [2]. The available management strategies at present mostly provide symptomatic relief but do not in general, address the disease process itself. The role of growth factors and autologous platelet-rich plasma (PRP) is recently being considered as a therapeutic possibility to augment healing of chondral injuries and modify the course of early degenerative arthritis. The concept that the application of PRP would improve cartilage repair is based on the physiological role of platelets in wound healing. There are over 1500 proteins within platelets including the growth factors like PDGF, VEGF, TGF-beta, FGF, and EGF that are known to play a pivotal role in the normal healing process [3]. The opposite treatment for cartilage injury remains a clinical challenge despite advances in surgical procedures and techniques. Even after promising preclinical findings and huge interest in its clinical application most questions on PRP remains unanswered.

Materials and Methods
This prospective study was conducted in MIMS Hospital, Andhra Pradesh on 50 patients of primary early OA diagnosed by American College of Rheumatology Criteria [4] after obtaining informed written consent and staged as per Ahlback's radiological grading [5]. Bilateral knee

involvement was seen in twelve patients making the final figure of 62 knees. The patients with Grade 1 and Grade 2 disease, aged 35-70 years, and no history of any intraarticular injection in the previous 3 months were included in the study.

The platelet-rich plasma was prepared from 100 ml patient's venous blood collected in 100 ml bag with CPD-A (Citrate Phosphate Dextrose and Adenine) as an anticoagulant. The blood was transferred into two 50 ml tubes which were then centrifuged for 15 minutes at 1500 rpm on a table top centrifuge. The blood was separated into platelet-rich plasma (PRP) and residual RBCs with the buffy coat. The PRP was extracted through a pipette and transferred to a test tube. It was then supplied in a syringe in a quantity of 8 ml meant for injection into one knee. The platelet concentrate was injected by a lateral approach by 18-20 Gauge needle. Patients were given a total of three injections at four weeks interval. Pre-injection and post-injection evaluation at three weeks, three months, and six months were done using VAS [6] and WOMAC [7] scores. Ahlback's grading wherever possible was done at six months.

Results

There was a total of 50 patients, of which 32 (64%) were females and 18 (36%) were males. The majority of the patients were in the age group of 51-60 years constituting 42%. 38 knees revealed grade 2 disease whereas grade 1 disease was seen in 12 knees. The age and sex distribution of patients are given in table 1.

Table 1: Age and sex distribution of patients.

Age (in years)	Females	Males	Total
<40	6	1	7(14.0%)
41-50	8	5	13 (26%)
51-60	12	9	21 (42%)
61-70	6	3	9 (18.0)
Total	32	18	50 (100%)

Individual mean WOMAC score and total mean WOMAC score were analyzed. Improvement in symptoms started showing up at 3 weeks which gradually improved over subsequent follow-ups and decrease in the mean values as shown in table 2.

VAS score decreased from 6.48 at pre-injection to 6.12, 4.34, and 3.56 at subsequent follow-ups till 6 months. The improvement seen was statistically significant. (Table 3).

The mean Total WOMAC score based on Ahlback's grading done at pre-injection and third follow up was calculated and it was observed that mean Total WOMAC score was less for grade 1 in comparison to grade 2 osteoarthritis. 18 patients had mild pain and 3 patients had moderate pain which subsided in 2-3 days without any intervention. No serious complication was encountered. The improvement as per patient version was asked at the end of six months. Almost 47 patients showed improvement though the level varied from mild to good improvement. (Table 4).

Discussion

In the current literature, only a handful of studies have studied the use of PRP in primary osteoarthritis of the knee. However, there is a lack of standardization among the available data. As a result, the evidence to support the clinical use of PRP as a treatment modality is uncertain in primary osteoarthritis of the knee. The mean age of patients in our study was 54.46 with a range of 35-70 years. Similar results were observed by Filardo *et al*. [8] and Patel *et al*., [9] whereas, in a study by Sanchez *et al*. [10] the mean age of the patients was 63.53 years which was because of the inclusion of advanced cases of osteoarthritis in their study.

We noted a female predominance in our study which is in agreement with the other studies.7, 8 However, in contrast, Kon *et al*. [11] and Sampson *et al*. [12] observed male preponderance in their study.

Pain is the most troublesome symptom, WOMAC and VAS score assessment revealed alike trends. Pain decreased significantly at first follow up which was comparable to the other published literature. However, the analysis of published data showed worsening at final 6 months follow up, which raises a question if the effect of PRP is provisional or it can modify the disease process or serial injections are required for long term relief? This is still an unanswered question and future research work is required to prove the same.

Sanchez *et al*. [10] in his study observed 33.3% success rate at week 5, Kon *et al*. [11] reported 80% satisfied patients and Patel *et al*. [9] had 67.3% satisfied patients in group A and 64% satisfied patients in group B at 6-month follow-up, in comparison with the control group in which only 4.3% were satisfied. Same results were validated in our study. The main complication was mild pain which was probably due to an interventional procedure and natural response of the body to inflammatory mediators.

We assume that platelet-rich plasma possibly has a role in the treatment of osteoarthritis which is supported by the improvement seen in VAS and WOMAC scores in our study at short term follow up. This improvement in our study is possibly due to the anti-inflammatory properties or due to the release of various growth factors and not because of chondral remodeling. If chondral remodeling was the cause for the improvement of symptoms, the benefit would have started later and lasted for a longer duration, however, to comment on the same in our study, longer follows up is needed. Furthermore, high-value studies with longer follow up are required to evaluate, if the effect of PRP is temporary or it can modify the disease process.

Limitations in our study were period and the evaluation parameters used which were WOMAC and VAS score only because pain is the main presenting symptom. Another drawback was lack of evidence if there is any cartilage regeneration as there were no follow up investigations other than X-ray which is not a sensitive device to document the change if there is any.

Table 2: WOMAC score (mean) at pre-injection, 3 weeks, 3 months and 6 months interval

Parameters	Pre injection	First follow up	Second follow up	Third follow up
Pain	15.28±3.04	13.63±2.37	7.98±2.67	6.02±3.31
Stiffness	6.16±1.52	4.81±1.61	2.86±1.42	2.01±1.21
Physical function	38.46±8.87	34.78±9.56	22.82±8.62	18.46±8.06
Total	58.68±11.86	51.96±10.74	34.42±9.04	26.51±10.28

Table 3: VAS score means with time

VAS score	Mean ±SD
Pre injection	6.48±1.18
1st follow up	6.12±1.2
2nd follow up	4.34±1.08
3rd follow up	3.56±1.17

Table 4: Status of improvement in patients at six months

Number of knees (N=62)	Satisfaction
21 (33.8%)	Good improvement
26 (41.9%)	Moderate improvement
11 (17.7%)	Mild improvement
04 (6.4%)	No improvement
-	Worsened

Conclusion

We conclude that it is evident that PRP is an effective treatment option for early grades of primary osteoarthritis of knee at short term follow up. However, more high value evidence based studies are required to prove its effectiveness on longer follow up and in late stages of OA cases.

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