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EFFECT OF PLATELET RICH PLASMA ON PAIN IN KNEE OSTEOARTHRITIS PATIETNS: A PILOT STUDY

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ABSTRACT **Aim:** To assess the effect of Platelet rich plasma (PRP) on knee osteoarthritis pain. Method: A total of 30 KL Grade 2/3 treatment-naïve patients with unilateral knee osteoarthritis for not more than 6 months were enrolled in the study. Autologous PRP was obtained from all the patients. Each patient was given 4-5 ml PRP at the affected knee. Baseline pain scores were noted on a 10-point visual analogue scale (VAS) scores. All the patients were called after one month. Patients failing to achieve a reduction in pain severity were given another PRP injection at the site. Final outcome was noted in terms of pain reduction at 3 months follow up. Data was analysed using SPSS 18.0 version. Wilcoxon signed rank test was used to compare the data. Results: Mean age of patients was 52.23±7.20 years (range 40-65 years), majority of patients were females (60%) and were urban residents (80%). Majority were homemakers or in service (60%). Mean BMI of patients was 27.4±3.97 kg/m2 (Range 20.2-35.0 kg/m2). Involvement of right side (56.7%) was more common. At enrolment 20 (66.7%) patients had moderate and 10 (33.3%) had severe pain. Mean pre-intervention VAS score was 6.17±0.95. Two PRP injections were required by 11 (36.7%) patients. At 3 months follow-up, 16 (53.3%) patients had mild pain and 14 (46.7%) had moderate pain. Mean VAS score at follow-up was 3.70±1.15. The change in pain score was significant statistically ($p<0.001$). Conclusion: PRP was useful in controlling pain in knee osteoarthritis patients in this short-term assessment.

KEYWORDS : Platelet rich plasma, Visual analogue scale, Knee osteoarthritis, KL Grade 2/3, Pain reduction

INTRODUCTION

Osteoarthritis (OA) finds the place as the fourth leading cause of disability[1]. It probably is the most common disease of joints in adults throughout the world[2]. More than 80% of osteoarthritis patients have involvement of knee[3] affecting nearly one-fifth of the population above the age of 45 years[4].

The clinical manifestation of disease includes pain, mobility restriction, and physical disability[5,6]. Among different clinical characteristics of knee OA, pain acquires the most important place. Pain primarily is responsible for mobility restriction and consequent physical disability[7]. With the advancement of disease contributing the increased movement disability the pain intensity changes from barely perceptible to extremely intolerable rendering the patient to a state of disability. Knee OA pain is characterized by exacerbation by activity and relief by rest. Most of the patients reporting for treatment of osteoarthritis complain of pain and relief in pain is the primary goal of treatment.

OA is a degenerative joint disease involving the articular cartilage and many of its surrounding tissues. In addition to damage and loss of articular cartilage, there is remodelling of subchondral bone, osteophyte formation, ligamentous laxity, weakening of periarticular muscles, and, in some cases, synovial inflammation[8].

Both pharmacological and non-pharmacological modalities are employed for treatment of Knee OA[9]. Pharmacological treatment modalities such as steroids are often associated with side effects. While surgical modalities involve processes of lavage and debridement in order to reduce synovitis and to improve joint motion, however, in the recent years its usefulness has been question in view of the results of large clinical trials showing no benefit for moderate to severe OA[10,11]. In general, it has been shown that for most patients with Knee OA surgery offers little benefit[12].

In recent years, the focus of knee OA management has shifted from use of pharmacological or surgical modalities to prevent cartilage degeneration and artircular structural remodelling and could revert back the process by initiating regenerative processes. In recent years, a preparation called Platelet rich plasma (PRP) is an emerging treatment modality classified as "Orthobiologics". Platelet Rich Plasma (PRP) is a natural concentrate of autologous blood growth factors in different fields of medicine in-order to test its potential to enhance tissue regeneration. Platelet rich-plasma has also been used for the treatment of osteoarthritis knee and has shown promising clinical and radiological outcomes[13,14], both in comparison to other pharmacological as well as non-pharmacological treatment modalities like physiotherapy[15-17].

In view of the projected benefits of PRP in management of knee OA, the present study was carried out to evaluate the effect of PRP use on knee osteoarthritis with focus on reduction in pain as the primary outcome.

MATERIAL AND METHOD

This study was carried out at orthopaedic clinic in a multispeciality hospital on 30 unilateral knee OA patients aged 40 to 65 years, diagnosed with radiological grade 2/3, having been diagnosed for knee OA for not more than six months with/without any history of conservative treatment (inclusion criteria). Patients with arthropathies, haematological disorders, having been on any intraarticular medication (steroids or Hyraluronic acid), having any active infection were excluded from the study (exclusion criteria). Informed consent was obtained from all the patients.

After enrolment demographic, anthropometric, clinical and radiological profile of patients was noted. Severity of pain was assessed using a 10-point VAS scale. Severity of pain was graded as – no pain (VAS score 0), mild pain (VAS score 1-3), moderate pain (VAS score 4-6) and severe pain (VAS score 7 or more).

A 20 ml of whole blood from all the consenting patients and autologous PRP was prepared as per procedure described by Dhurat and Sukesh[18]. After the preparation of PRP, 5 ml of PRP was injected in knee through supralateral approach with an 22-gauge needle. Knee immobilized for 8-10 minutes and discharged after half an hour of observation. Tablet paracetamol (650 mg) was given stat in patients who experienced pain at injection site after 10 minutes. All patients were asked to stop medications 48 hrs before follow up assessment.

All the patients was asked to appear report for development of any complication telephonically to the investigator and were followed up one week, one month and three months after intervention. Pain intensity was measured on VAS scale at each follow-up. Repeat PRP injection intervention was done on those patients who did not show a change in pain grade following intervention at one month. Final outcome was noted at 3 months.

Statistical Analysis

The data collected from the patients was fed into MS-Excel software. Statistical analysis was done using Statistical Package for Social Sciences (SPSS) 18.0 version. Wilcoxon signed rank test was used to evaluate the significance of change in pain scores. A 'p' value less than 0.05 was considered significant.

RESULTS

Age of patients ranged from 40 to 65 years. Mean age of patients was 52.23±7.20 years. Majority of patients were females (60%). The sex

ratio of study population was 0.67. Most of the patients were urban residents (80%) only 6(20%) were from rural areas. Maximum (40%) were homemakers followed by those in service (20%), teachers (16.7%), shop-owners (13.3%), businessmen (6.7%) and retired (3.3%) personnel. Right side (56.7%) was more commonly involved than the left side (43.3%). BMI of patients ranged from 20.2 to 35.0 kg/m^2 and mean BMI was 27.4±3.97 kg/m^2. Exactly half the patients were of KL grade 2 and 3 respectively. Only 11 (36.7%) patients required two PRP injections (Table 1).

At enrolment 20 (66.7%) patients had moderate and 10 (33.3%) had severe pain. Mean pre-intervention VAS score was 6.17±0.95. At final follow-up majority (53.3%) had mild pain and remaining 14 (46.7%) had moderate pain. Mean post-intervention VAS score was 3.70±1.15. The change in pain score was significant statistically ($p<0.001$) (Table 2; Fig. 1).

No side effect/complication was noted in 27 (90%) cases. There was one patient (3.3%) who reported of transient pain while 2 (6.7%) developed transient pain with synovitis (Table 3).

Overall, a total of 20 (66.7%) patients showed downgrading of pain (10/20 patients with moderate pain at baseline shifted to mild pain at final follow-up; 6/10 with severe pain shifted to mild pain at final follow-up and 4/10 with severe pain at baseline shifted to moderate pain at final follow-up). No change in pain grade was observed in 10 (33.3%) cases. None of the cases showed upgradation of pain (Table 4).

DISCUSSION

The present study showed an urban, female dominated profile of patients having high BMI and mainly performing sedentary work. This is in agreement with epidemiological studies reporting female sex, urban sedentary life and obesity to be risk factors for development of OA[19,20].

In present study, we found downgrading of pain in majority (66.7%) cases and an overall significant change in mean VAS scores (6.17 to 3.70; 40% reduction). A number of other studies have shown sustenance of improvement in functional outcomes and reduction in pain[13,21,22]. Similar to findings of present study, Hassan *et al.*[22] also showed a decline in mean VAS score from 5.9 ± 1.3 at baseline to 3.9 ± 1.1 at follow-up. Kanchanatawan *et al.*[23] in a meta-analysis of nine studies also reported that PRP injections were successful to bring about a significant change in pain as observed in present study. Di *et al.*[24] also while comparing Hyaluronic acid to PRP for treatment of knee osteoarthritis in a systematic review that included 908 patients and 908 knees reported statistically significant improvements in clinical outcomes, including pain, physical function, and stiffness, with PRP treatment and found it to be comparable to HU. The present study also showed that PRP is useful in management of knee OA related pain with the use of autologous PRP with minimum side effects.

In present study, we noticed side effects – transient pain at injection site and transient pain+synovitis in only three cases, thus showing PRP to be a safe drug. These are minor complications that are resolved on their own. In their study, Elksniņš-Finogejevs *et al.*[25] reported mild synovitis following injection of PRP in 75% of patients but reported self resolution in all the cases, hence showing that these mild complications have no clinical value.

Considering the fact that pain happens to be most common reason for disability among knee OA patients, resolution of pain using PRP could be considered to be a contributory step towards reducing the burden of this disease. Though in present study owing to shortage of resources and paucity of time the outcomes were restricted to only evaluation of pain reduction, however , given regenerative nature of PRP, it might also be expected that it would be helpful in reconstruction of degenerated tissues[13,14]. Further studies focusing on other comprehensive outcomes are also recommended.

CONCLUSION

The findings in present study, like previous studies endorse the usefulness of PRP in treatment of knee osteoarthritis with relief in pain as the primary outcome. One of the limitations of present study was short duration of follow-up (3 months only) and small sample size, hence further studies on a larger sample size with longer duration of follow-up are recommended.

Table 1: Demographic Profile and Patient Characteristics

SN	Variable	Statistic
1.	Mean age±SD (Range) (Years)	52.23±7.20 (40-65)
2.	Sex	
	Male	12 (40.0%)
	Female	18 (60.0%)
3.	Habitat	
	Rural	6 (20.0%)
	Urban	24 (80.0%)
4.	Mean BMI±SD (Range) (kg/m^2)	27.4±3.97 (20.2-35.0)
5.	Occupation	
	Homemaker	12 (40.0%)
	Service	6 (20.0%)
	Teacher	5 (16.7%)
	Shop owner	4 (13.3%)
	Businessman	2 (6.7%)
	Retired	1 (3.3%)
6.	Side involved	
	Left	13 (43.3%)
	Right	17 (56.7%)
7.	KL Grade	
	2	15 (50.0%)
	3	15 (50.0%)
8.	No. of PRP Injections needed	
	One	19 (63.3%)
	Two	11 (36.7%)

Table 2: Pre- and Post-Intervention Comparison of Pain (VAS Score)

SN	Severity of Pain (VAS Score)	Pre-intervention	Post-intervention
1.	No pain (0)	0	0
2.	Mild pain (1-3)	0	16 (53.3%)
3.	Moderate pain (4-6)	20 (66.7%)	14 (46.7%)
4.	Severe pain (≥7)	10 (33.3%)	0
Mean VAS score±SD (Range)		6.17±0.95 (5-8)	3.70±1.15 (2-6)

$z=4.652$; $p<0.001$ (Wilcoxon signed rank test)

Table 3: Side effects / Complications

SN	Variable	No.	%
1.	Transient pain	1	3.3
2.	Transient pain + Synovitis	2	6.7
3.	No complication	27	90.0

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