Section: Orthopedics

Original Research Article

CLINICAL STUDY ON EFFICACY OF PLATELET RICH PLASMA INJECTION IN THE MANAGEMENT OF EARLY OSTEOARTHRITIS OF KNEE JOINT

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ABSTRACT

Background: Knee osteoarthritis (OA) affects approximately 260 million people worldwide and is a common cause of disability. Effective and safe medical treatments are needed. Currently, no approved disease-modifying drugs exist, and non-operative therapies are associated with only small to moderate benefits and may have serious adverse effects. Platelet-rich plasma (PRP) is a safe autologous blood product containing high levels of growth factors and cytokines with potential to alter biological processes implicated in OA pathogenesis and symptoms. **Objective:** The aim of this study is to determine the clinical efficacy of Intraarticular PRP injection in early osteoarthritis of knee joint.

Materials and Methods: A prospective, single blinded, randomized control trial in 100 Patients of Karnataka Medical College & Research Institute, Hubballi with early (Grade 1 and 2 Kellgren-Lawrence classification) osteoarthritis of knee joint in patients between 40 – 65 years of age treated with platelet rich plasma injection. Demographic data, history, Clinical examination and details of investigations will be recorded in the study proforma.

Results: Intraarticular PRP was injected into 100 patients. The most common age group involved in study is 56-60 years (28%) with 54 (54%) patients were male and M:F ratio of 1.17. There is a statistically significant difference between the mean values of VAS, KOOS, WOMAC and OK Scores at 6 months compared to baseline scores without any serious adverse effect.

Conclusion: The outcomes of this study showed that the use of PRP injections for treating OA (Grade 1 and 2 Kellgren-Lawrence classification) were shown to be successful in terms of improving functional results and diminishing pain intensity. PRP holds a promising, effective, better solution in the management in OA knee.

Keywords: Osteoarthritis, VAS, WOMAC, KOOS, OKS, Kellgren Lawrence Classification, Platelet rich plasma.

INTRODUCTION

Osteoarthritis [OA] is a complex whole joint, chronic, degenerative disease caused by inflammatory mediators rather than purely a process of wear and tear. OA is a most common joint disease in India and major cause of pain and disability in adults.[1] Recent studies have shown that the incidence of OA of knee is increasing compared to other joints, especially in young adults. Bilateral knee OA is more common than unilateral disease, affecting 5% versus 2%, respectively, of persons 45 to 74 years of age.[2] Having OA in one knee increases the likelihood of having OA in the contralateral knee.[3] It is believed that tibiofemoral OA is more common than patellofemoral OA.

OA is usually classified as primary (idiopathic) or secondary to metabolic conditions, anatomic abnormalities, trauma, or inflammatory arthritis.

The prevalence of radiographic knee OA rises in women from 1% to 4% in those 24 to 45 years of age to 53% to 55% in those of age 80 years and older. In men, the prevalence rises from 1% to 6% in those 45 years and younger to 22% to 33% in those 80 years.[4]

Currently treatment of OA mainly focuses on relieving of symptoms and improving day to day physical activities. Non pharmacological modalities are patient education, weight reduction, exercises, walking support, shoes and insole modifications. Pharmacological therapy includes non-steroidal anti-inflammatory drugs, opioids, and slow acting drugs like glucose amine and chondroitin sulphate. Intra articular injections like platelet rich plasma (PRP), corticosteroids, hyaluronic acid, autologous mesenchymal stem cells.[5]

Corticosteroid have both anti-inflammatory and immune suppressive effect. They act directly on nuclear steroid receptor and interrupt the inflammatory and immune cascade at many levels. They reduce vascular permeability and inhibit accumulation of inflammatory cells, phagocytosis, production of neutrophils, superoxides, and prevent the synthesis and secretion of several inflammatory mediators like prostaglandins.[6]

With widespread increase in research in the field of regenerative orthopedics, PRP has become viable, biological and natural healing enhancer. PRP is an orthobiological agent that has high concentration of platelets (above baseline) with the aim of accelerating tissue healing, modulating inflammation, and providing symptomatic relief. PRP releases supra-physiological levels of growth factors and other bioactive molecules.[7]

Dense-core granules in platelets contain ADP, Thromboxane A2, 5-hydroxytryptamine, histamine, adrenaline and Ca2+, all of which are critical for further platelet activation. Once activated they degrade alpha granule which release Transforming growth factor-beta, Platelet derived growth factor (PDGF), Insulin like growth factors 1 and 2, fibroblast growth factor (FGF), Epidermal growth factor (EGF), Vascular endothelial growth factor (VEGF) and many more. Once the growth factor binds to the target cell receptor, it induces an intracellular signal transduction system and produces a biological response critical for chemotaxis, cell proliferation and osteoblastic differentiation.[8]

Hence this study was conducted on autologous platelet rich plasma intraarticular injection in patient with early osteoarthritis of knee.

MATERIALS AND METHODS

This a prospective study includes 100 cases of early osteoarthritis of knee joint seen at Karnataka Medical College & Research Institute (KMCRI), Hubballi. Study period was 2 years (July 2022 to July 2024)

Sample size: 100 patients

Inclusion Criteria

- Age between 40-65years.
- Diagnosis of Grade I and Grade II (Kellgren-Lawrence classification) osteoarthritis of knee joint.

Exclusion Criteria

- Patients below 40 yrs. and above 65 years.
- Infection or tumor at the site of therapy application, Severe blood dyscrasia
- Blood-clotting disorders, Treatment with oral anticoagulants.
- Received intra-articular injections of steroids, anaesthetics, or hyaluronic acid in the past year

Methodology:

After getting Institutional Ethical Committee clearance and Informed Consent, patients from the OPD of Department of Orthopaedics, Karnataka Medical College & Research Institute (KMCRI), Hubballi were included in the study.

Demographic data of patient, brief medical history was taken, along with Clinical Examination for all the patients participated in study was done.

Radiological Investigation and OA Staging-Anteroposterior and Lateral Radiographs of Knees in standing position was done for all patients.

- Based on Kellgren-Lawrence system of grading, the radiological staging of OA was done for each patient.
- Patient's VAS, KOOS, WOMAC and OKS score were noted before procedure.
- Patients were administered with Single shot of Intra articular Platelet rich plasma (PRP) injection
- After the injection, for pain relief paracetamol/paracetamol+tramadol was used.
- Post treatment physiotherapy was advised. The data will be recorded in the appropriate proforma.
- The patients will be evaluated for Visual analogue score (VAS), KOOS, WOMAC and OKS score at regular follow up at the end of 2nd week, 4th week, 6th week, 3 months and 6 months.
- Patients were trained for home based active quadriceps and knee strengthening exercises.
- Patient were advised to weight bear immediately.

Post procedure protocol: Patients were advised for paracetamol / paracetamol + tramadol as analgesics. Patients were allowed to go home and weight bearing was allowed immediately.

Follow up: Patients were followed up at 2nd week, 4th week, 6th week, 3 months and 6 months after administration of Autologous Platelet rich plasma (PRP). During the follow up visit, patient's Brief Clinical History, Clinical Examination was done.

The patients were then evaluated for clinical improvement by using,

- Visual Analogue Scale (VAS)
- The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale.
- The Knee Injury and Osteoarthritis Outcome score (KOOS)
- Oxford Knee Score (OKS)

Statistical Analysis: Data collected was entered in MS Office Excel and analyzed using Statistical package software [SPSS 29.0]. Statistical methods used include descriptive statistics (Percentages and Mean). Repeated ANOVA measures of significance was used to find the association between the categorical variables namely Age group, Sex, Grade of OA, Site involvement. Independent-t test was used to find out statistically significant difference between the mean values of Visual analogue score (VAS), The Knee Injury and Osteoarthritis Outcome score (KOOS), The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale and Oxford Knee Score (OKS). P-value <0.05 is considered as statistically significant.

RESULTS

100 patients were included in the study. 100 patients were given intra articular PRP injection and followed up for 6 months. The patients were evaluated clinically and statistically.

Our study has most of the patients in the age group of 56-60 years i.e. 28 (28%) patients, followed by 46-50 years i.e. 23 (23%) patients, 61-65 years i.e. 20 (20%), 51-55 years i.e. 18 (18%) patients, and 41-45 years i.e. 11 (11%) patients with mean age of 54.17 years.

In our study out of total 100 patients, 46 (46%) patients were females and 54 (54%) patients were males with Male: Female ratio of 1.17

In our study out of 100 patients, 49 (49%) patients had left side involvement and 51 (51.0%) patients had right side involvement.

In our study out of 100 patients, 53 (53%) patients belong to Grade I of Osteoarthritis of knee and 47 (47%) patients belong to Grade II Osteoarthritis of knee according to Kellgren Lawrence Classification.

This table represents the VAS scores at six different time points: Pre-injection and at intervals post-injection i.e. 2 weeks, 4 weeks, 6 weeks, 3 months, and 6 months after intra-articular PRP injection.

- The average VAS score before the injection is 7.06, with a standard deviation of 1.05. This shows that the participants reported high levels of pain, with most scores falling around the mean.
- The mean score decreases to 6.99 in 2 weeks of post injection and there is further decrease noted in mean score at the end of 4th and 6th with 6.15 and 5.58 mean scores respectively i.e. showing the significant pain relief.

By the end of 3 months and 6 months the mean scores reduced still further to 4.86 and 3.96 indicating the sustained pain relief over time. [Table 1]

The following table gives us information about statistical examination of the data using Repeated Measures ANOVA for significant differences

- The mean scores decrease steadily from 7.06 at baseline to 3.96 at 6 months with the standard deviation (SD) increases slightly over time, from 1.052 at baseline to 1.399 at 6 months which suggests that while the average pain level decreases, there is increasing variability in how participants respond over time.

Repeated Measures ANOVA with $p<0.005$ (Sig.) This result indicates that the differences in VAS scores over time are statistically significant confirming that the intervention had a significant impact on reducing pain. [Table 2]

- The analysis shows that there is a significant reduction in pain from baseline at all time points beyond the 2nd week post-injection.
- The p-values indicate that these changes are highly statistically significant, confirming the effectiveness of the intervention over time. [Table 3]

This table represents the WOMAC scores at six different time points: Pre-injection and at intervals post-injection i.e. 2 weeks, 4 weeks, 6 weeks, 3 months, and 6 months after intra-articular PRP injection. [Table 4]

- The average WOMAC score before the injection is 47.19, with a standard deviation of 7.87. This shows that the participants reported high levels of pain and worsening knee function with most scores falling around the mean.
- The mean score decreases to 43.76 in 2 weeks of post injection and there is further decrease noted in mean score at the end of 4th and 6th with 40.34 and 36.52 mean scores respectively i.e. showing the significant decrease in pain and improved knee function.
- By the end of 3 months and 6 months the mean scores reduced still further to 32.44 and 28.20 indicating the sustained pain relief and improving knee function over time.

The following table gives us information about statistical examination of the data using Repeated Measures ANOVA for significant differences. [Table 5]

- The mean scores decrease steadily from 47.19 at baseline to 28.20 at 6 months with the standard deviation (SD) increases slightly over time, from 7.87 at baseline to 8.63 at 6 months which suggests that while the average pain level decreases, there is increasing variability in how participants respond over time.
- Repeated Measures ANOVA with $p<0.005$ (Sig.). This result indicates that the differences

in WOMAC scores over time are statistically significant confirming that the intervention had a significant impact on reducing pain and improve in knee function.

- The analysis shows that there is a significant reduction in pain from baseline at all time points
- The p-values indicate that these changes are highly statistically significant, confirming the effectiveness of the intervention over time. [Table 6]

This table represents the KOOS scores at six different time points: Pre-injection and at intervals post-injection i.e. 2 weeks, 4 weeks, 6 weeks, 3 months, and 6 months after intra-articular PRP injection. [Table 7]

- The average KOOS score before the injection is 32.02, with a standard deviation of 10.08. This shows that the participants reported high levels of pain and worsening knee function with most scores falling around the mean.
- The mean score increases to 37.70 in 2 weeks of post injection and there is further increase observed in mean score at the end of 4th and 6th with 42.27 and 46.64 mean scores respectively i.e. showing the significant decrease in pain and improved knee function.
- By the end of 3 months and 6 months the mean scores increased still further to 51.27 and 53.48 indicating the sustained pain relief and improving knee function over time.

The following table gives us information about statistical examination of the data using Repeated Measures ANOVA for significant differences. [Table 8]

- The mean scores increase steadily from 32.02 at baseline to 53.48 at 6 months with the standard deviation (SD) decreasing over time, from 10.08 at baseline to 7.24 at 6 months which suggests that while the average pain level decreases, there is increasing variability in how participants respond over time.
- Repeated Measures ANOVA with $p<0.005$ (Sig.). This result indicates that the differences in KOOS scores over time are statistically significant confirming that the intervention had a significant impact on reducing pain and improve in knee function.
- The analysis shows that there is a significant reduction in pain from baseline at all time points
- The p-values indicate that these changes are highly statistically significant, confirming the effectiveness of the intervention over time.

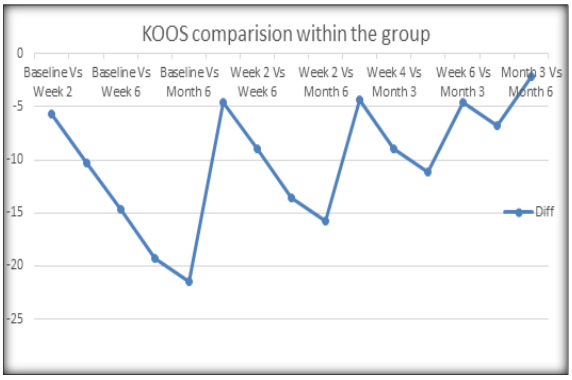

Figure 1: Graphical representation of within the KOOS group comparison

This table represents the OKS scores at six different time points: Pre-injection and at intervals post-injection i.e. 2 weeks, 4 weeks, 6 weeks, 3 months, and 6 months after intra-articular PRP injection. [Table 9]

- The average OKS score before the injection is 17.25, with a standard deviation of 5.99. This shows that the participants reported high levels of pain and worsening knee function with most scores falling around the mean.
- The mean score increases to 19.56 in 2 weeks of post injection and there is further increase observed in mean score at the end of 4th and 6th with 21.87 and 24.62 mean scores respectively i.e. showing the significant decrease in pain and improved knee function.

By the end of 3 months and 6 months the mean scores increased still further to 27.95 and 30.43 indicating the sustained pain relief and improving knee function over time.

The following table gives us information about statistical examination of the data using Repeated Measures ANOVA for significant differences

- The mean scores increase steadily from 17.25 at baseline to 30.43 at 6 months with the standard deviation (SD) decreasing over time, from 5.99 at baseline to 4.82 at 6 months which suggests that while the average pain level decreases, there is increasing variability in how participants respond over time.
- Repeated Measures ANOVA with $p<0.005$ (Sig.). This result indicates that the differences in OKS scores over time are statistically significant confirming that the intervention had a significant impact on reducing pain and improve in knee function.

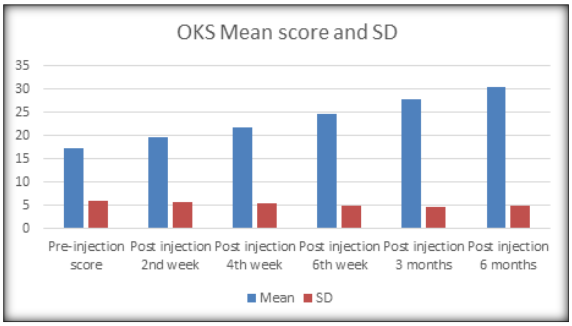

Figure 2: Graphical representation of OKS (Mean and SD)

- The analysis shows that there is a significant reduction in pain from baseline at all time points
- The p-values indicate that these changes are highly statistically significant, confirming the effectiveness of the intervention over time.

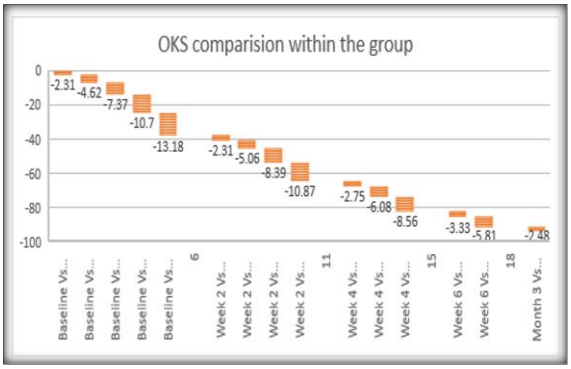

Figure 3: Graphical representation of within the KOOS group comparison

- This table of VAS, KOOS, WOMAC, and OKS scores showed female and male patients to improve significantly with knee pain, function, and overall symptoms after knee injections.
- Though there was a little difference in all scores between the two sexes, it did not reach any statistical significance, thereby proving treatment impartial for the females and males.
- This implies that gender did not have a pivotal role in the results in six months of follow up after knee injections were given. [Figure 3]
- This table of VAS, KOOS, WOMAC, and OKS scores showed Kellgren-Lawrence Grade I and Grade II osteoarthritis of Knee patients to improve significantly with knee pain, function, and overall symptoms after knee injections.
- Though there was a little difference in all scores between the two grades, it did not reach any statistical significance, thereby proving treatment impartial for the both grades.
- This implies that grade of osteoarthritis did not have a pivotal role in the results in six months of follow up after knee injections were given. This table of VAS, KOOS, WOMAC, and OKS scores showed both left and right knee affected patients to improve significantly with knee pain, function, and overall symptoms after knee injections.
- Though there was a little difference in all scores between the two sides, it did not reach any statistical significance, thereby proving treatment impartial for both sides.
- This implies that side of the knee involved did not have a pivotal role in the results in six months of follow up after knee injections were given.

Table 1: Statistical analysis of VAS score

VAS Score	Mean (SD)	Median (IQR)	Min	Max
Pre-injection score	7.06 (1.05)	7 (6-8)	5	9
Post injection 2nd week	6.99 (1.06)	7 (6-8)	5	9
Post injection 4th week	6.15 (1.07)	6 (5-7)	4	8
Post injection 6th week	5.58 (1.16)	5 (5-6)	3	8
Post injection 3 months	4.86 (1.33)	5 (4-6)	2	8
Post injection 6 months	3.96 (1.40)	4 (3-5)	1	7

Table 2: Statistical analysis of VAS score (Mean and SD)

VAS Score	N	Mean	SD	Repeated Measures ANOVA
Pre-injection score	100	7.06	1.052	p<0.005 (Sig.)
Post injection 2nd week	100	6.99	1.059	
Post injection 4th week	100	6.15	1.067	
Post injection 6th week	100	5.58	1.165	
Post injection 3 months	100	4.86	1.333	
Post injection 6 months	100	3.96	1.399	

Table 3: Statistical analysis of VAS score

VAS Comparison	Diff	P value
Baseline Vs Week 2	0.07	0.283
Baseline Vs Week 4	0.91	<0.005 (Sig.)
Baseline Vs Week 6	1.48	<0.005 (Sig.)
Baseline Vs Month 3	2.2	<0.005 (Sig.)
Baseline Vs Month 6	3.1	<0.005 (Sig.)
Week 2 Vs Week 4	0.84	<0.005 (Sig.)

Week 2 Vs Week 6	1.41	<0.005 (Sig.)
Week 2 Vs Month 3	2.13	<0.005 (Sig.)
Week 2 Vs Month 6	3.03	<0.005 (Sig.)
Week 4 Vs Week 6	0.57	<0.005 (Sig.)
Week 4 Vs Month 3	1.29	<0.005 (Sig.)
Week 4 Vs Month 6	2.19	<0.005 (Sig.)
Week 6 Vs Month 3	0.72	<0.005 (Sig.)
Week 6 Vs Month 6	1.62	<0.005 (Sig.)
Month 3 Vs Month 6	0.9	<0.005 (Sig.)

Table 4: Statistical analysis of WOMAC score

WOMAC Scores	Mean (SD)	Median (IQR)	Min	Max
Pre-injection score	47.19 (7.87)	47.50 (40-53)	28	65
Post injection 2nd week	43.76 (7.43)	45 (37-50)	25	63
Post injection 4th week	40.34 (7.13)	41 (35-46)	24	62
Post injection 6th week	36.52 (7.60)	36 (31-41)	22	62
Post injection 3 months	32.44 (8.19)	30 (27-36)	20	60
Post injection 6 months	28.20 (8.63)	26 (22-30)	18	59

Table 5: Statistical analysis of WOMAC score (Mean and SD)

WOMAC Scores	N	Mean	SD	Repeated Measures ANOVA
Pre-injection score	100	47.19	7.87	**p<0.005 (Sig.)**
Post injection 2nd week	100	43.76	7.43	
Post injection 4th week	100	40.34	7.13	
Post injection 6th week	100	36.52	7.6	
Post injection 3 months	100	32.44	8.19	
Post injection 6 months	100	28.2	8.63	

Table 6: Statistical analysis of WOMAC score (Within group comparison)

WOMAC Comparison	Diff	P value
Baseline Vs Week 2	3.43	**<0.005 (Sig.)**
Baseline Vs Week 4	6.85	**<0.005 (Sig.)**
Baseline Vs Week 6	10.67	**<0.005 (Sig.)**
Baseline Vs Month 3	14.75	**<0.005 (Sig.)**
Baseline Vs Month 6	18.99	**<0.005 (Sig.)**
Week 2 Vs Week 4	3.42	**<0.005 (Sig.)**
Week 2 Vs Week 6	7.24	**<0.005 (Sig.)**
Week 2 Vs Month 3	11.32	**<0.005 (Sig.)**
Week 2 Vs Month 6	15.56	**<0.005 (Sig.)**
Week 4 Vs Week 6	3.82	**<0.005 (Sig.)**
Week 4 Vs Month 3	7.9	**<0.005 (Sig.)**
Week 4 Vs Month 6	12.14	**<0.005 (Sig.)**
Week 6 Vs Month 3	4.08	**<0.005 (Sig.)**
Week 6 Vs Month 6	8.32	**<0.005 (Sig.)**
Month 3 Vs Month 6	4.24	**<0.005 (Sig.)**

Table 7: Statistical analysis of KOOS score

KOOS score	Mean (SD)	Median (IQR)	Min	Max
Pre-injection score	32.02 (10.08)	28 (26-35)	21	61
Post injection 2nd week	37.70 (8.99)	35 (31-43)	26	62
Post injection 4th week	42.27 (7.67)	40 (37-46)	28	63
Post injection 6th week	46.64 (7.24)	46 (41-50)	31	64
Post injection 3 months	51.27 (7.53)	50 (46-55)	36	67
Post injection 6 months	53.48 (7.24)	52.50 (49-59)	39	70

Table 8: Statistical analysis of KOOS score (Mean and SD)

KOOS score	N	Mean	SD	Repeated Measures ANOVA
Pre-injection score	100	32.02	10.08	**p<0.005 (Sig.)**
Post injection 2nd week	100	37.7	8.99	
Post injection 4th week	100	42.27	7.67	
Post injection 6th week	100	46.64	7.24	
Post injection 3 months	100	51.27	7.53	
Post injection 6 months	100	53.48	7.24	

Table 9: Statistical analysis of OKS score

KOOS score	Mean (SD)	Median (IQR)	Min	Max
Pre-injection score	17.25 (5.99)	15 (14-18)	10	38
Post injection 2nd week	19.56 (5.60)	18 (16-21)	13	37
Post injection 4th week	21.87 (5.40)	20 (18-24)	16	38
Post injection 6th week	24.62 (4.91)	23 (21-28)	17	39
Post injection 3 months	27.95 (4.54)	28 (24-31)	18	38
Post injection 6 months	30.43 (4.82)	30 (26-34)	20	40

Table 10: Statistical analysis of scores between grades

VAS Score	Grade 1	Grade 2	Mean Diff	P value
Pre-injection score	7.075	7.043	0.033	0.877
Post injection 2nd week	6.981	7	-0.019	0.93
Post injection 4th week	6.132	6.17	-0.038	0.859
Post injection 6th week	5.472	5.702	-0.23	0.326
Post injection 3 months	4.755	4.979	-0.224	0.405
Post injection 6 months	3.83	4.106	-0.276	0.327
KOOS score				
Pre-injection score	31.094	33.064	-1.969	0.332
Post injection 2nd week	36.717	38.809	-2.092	0.248
Post injection 4th week	41.415	43.234	-1.819	0.238
Post injection 6th week	46	47.362	-1.362	0.351
Post injection 3 months	50.66	51.957	-1.297	0.393
Post injection 6 months	53	54.021	-1.021	0.485
WOMAC score				
Pre-injection score	47.491	46.851	0.64	0.687
Post injection 2nd week	44.264	43.191	1.073	0.474
Post injection 4th week	40.415	40.255	0.16	0.912
Post injection 6th week	36.396	36.66	-0.263	0.864
Post injection 3 months	32.34	32.553	-0.214	0.897
Post injection 6 months	27.981	28.447	-0.466	0.789
OKS score				
Pre-injection score	16.453	18.149	-1.696	0.159
Post injection 2nd week	18.925	20.277	-1.352	0.23
Post injection 4th week	21.132	22.702	-1.57	0.148
Post injection 6th week	23.962	25.362	-1.399	0.156
Post injection 3 months	27.415	28.553	-1.138	0.213
Post injection 6 months	29.962	30.957	-0.995	0.305

DISCUSSION

Current literature suggests that that intra articular knee injection is a promising modality in managing pain associated with OA knee. It is a well-tolerated, minimally invasive intervention, especially in patients with co-morbidities, who neither have the fitness for the surgery nor able to tolerate oral analgesics for a long-term period. Various Intra articular injectables like corticosteroids, infliximab, hyaluronic acid, botulinum neurotoxin, PRP, and even stem cells are being used in the management of knee osteoarthritis.[1,9,10]

Last few years, there is growing interest in exploring PRP as a treatment modality for OA knee. The platelet concentrate in PRP when activated results in the formation of platelet gel and the release of growth factors and bioactive molecules which effectively participate in the healing process. Platelets contain significant amounts of cytokines and growth factors and are responsible for stimulating cellular growth, vascularization, proliferation, tissue regeneration, and collagen synthesis. A regenerative therapy that is believed to promote healing by augmenting and accelerating the natural healing cascade. The Injection of PRP to treat OA of the knee can be considered a relatively new therapeutic indication.[11]

The platelet rich plasma acts as a minimally invasive procedure which bridges the gap between pharmacological treatment and surgical treatment for osteoarthritis. It provides a strong and positive balance between pro-apoptotic and anti-apoptotic molecules, pro-inflammatory and anti-inflammatory cytokines & pro-angiogenic and anti-angiogenic factors for rejuvenation of degenerated cartilaginous tissues. Once PRP is activated, plasma fibrinogen polymerizes into a 3D fibrin scaffold, which contains heparan sulphate binding domains for growth factors, cytokines, chemokines, ECM components, cell adhesion molecules and acute phase proteins. This biodegradable 3D scaffold provides plastic-elastic stiffness and generates growth factors for cell proliferation, differentiation and migration. Once injected into the joint, 3D scaffold is converted into a viscous and malleable structure and further fibrinolysis begins and sustained release of growth factors occurs.[12]

The growth factors rejuvenate the cartilage by producing IL-1Ra and other anti- apoptotic, anti-inflammatory and pro-angiogenic factors. The platelet rich plasma upregulates tissue inhibitor of metalloproteinases such as TIMPs -1, -3 and -4 by downregulating the signalling molecules of matrix

metalloproteinases such as MMP-1, MMP-3, MMP-13 & MMP-28 and upregulation of ADAMTS-4 and 5 which leads to normal joint homeostasis.[13]

Pain Reduction and Functional Improvement

This mean change from baseline to six months was significantly reduced with regard to pain. This result agrees with previous literature that has shown the efficacy of different treatment modalities, including conservative management, pharmacological interventions, and surgical options in reducing pain in patients suffering from knee OA. For example, Bannuru et al,[14] conducted a meta-analysis in 2019 comparing the various interventions, which suggested both pharmacological and non-pharmacological treatments decreased pain with an attenuated effect size at the longer follow-up. More importantly, besides the findings of the current study, this progressive decrease of VAS scores further indicates the necessity of long-term and continuous treatment efforts in patients with knee OA.

Functional outcomes, measured by the KOOS, WOMAC, and OKS, also improved significantly over time. The results therefore support prior studies in demonstrating that the treatment protocols are effective in enhancing knee-related function and improving general quality of life. In a study on exercise therapy with education in patients diagnosed with knee OA by Skou et al. (2015),[15] functional scores improved over the 12-month follow-up period, but more remarkable gains were seen in the first few months of treatment. This is consistent with the results of this present study, whereby maximum functional improvements have been noted in the first six months, thereby once again proving the point that early institution of treatment and regular follow-up are important.

Gender, Grade, and Side Comparisons

No significant differences in pain decrease or functional improvement were noted between male and female patients with knee OA. This is interesting since previous literature on possible gender differences in knee OA outcomes is still quite mixed. For example, Hunter et al. (2014),[16] suggested that women might suffer from more severe pain and poor functional outcomes compared to men, which may be related to differences in biomechanics, sex hormones, and pain perception. However, the findings of this present study show that with comparable treatment guidelines, both genders can have similar results, proving that the therapeutic protocols are blind to gender and should be the same in both knee OA patients.

For the disease grade, those patients who have Grade 2 knee OA reported slightly worse pain and functional scores compared to those with Grade 1, though these differences did not reach statistical significance. This trend is similar to that described by Hinman et al. (2010),[17] whereby higher grades of the disease are often associated with greater severity of symptoms and reduced functional capacity. The insignificant differences noted in the present study could be a function of a relatively short period of follow-up or the effectiveness of the treatment protocol in attenuating the impact of disease severity on outcomes.

Outcomes were compared based on whether patients had left knee versus right knee involvement; again, no significant differences were identified. This finding is in line with other studies, like one by Culvenor et al. in 2017,[18] which stated that the side of knee involvement does not impact the pain or functional results of patients with knee OA. Thus, treatment schemes can be effective regardless of whether the left or the right knee has the disorder. This lends further to the generalization of the present study's findings.

CONCLUSION

The study provides a comprehensive evaluation of the effectiveness of Intra-articular Platelet rich plasma in managing early osteoarthritis of Knee (Grade I and II of Kellgren-Lawrence classification). Patients demonstrated significant pain relief and improved functional ability over the period of intervention. The results emphasized the effectiveness of treatment in sustaining the benefits over the six-month follow-up period. There were no significant differences observed in relation to gender, grade of condition, or affected side; hence, further supports the generalization of results related to treatment outcome across different patient demography.

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