

EFFICACY OF AUTOLOGOUS PLATELET-RICH PLASMA INJECTION IN KNEE OSTEOARTHRITIS

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Abstract

Background: Platelet-rich plasma (PRP) is believed to aid in the healing of various conditions including osteoarthritis. Additionally, the recurrence rate of these conditions after PRP treatment is expected to be low. In this study, we will be administering intralesional injections of autologous PRP to treat knee osteoarthritis. **To study the efficacy of autologous platelet-rich plasma in knee osteoarthritis. Materials and Methods:** A year-long randomized, open, prospective, and comparative study was conducted on 30 patients who visited the Orthopedics outpatient department of Varun Arjun Medical College from March 2023 to February 2024. The patients were selected based on meeting the inclusion and exclusion criteria after obtaining ethical clearance. The patients underwent a standardized injection protocol and were evaluated for pain, stiffness, and physical function using the Western Ontario and McMaster Universities Arthritis Index (WOMAC) scale before the injection, as well as at 6 weeks, 3 months, and 6 months after the injection for Osteoarthritis knee. Statistical tests used were Mean, Median, Interquartile Range (IQR), Standard Deviation (SD), Analysis of variance (ANOVA), Friedman test and Wilcoxon signed rank test. **Result:** Patients suffering from knee osteoarthritis reported complete pain relief after six months of platelet-rich plasma injections with no complications or side effects. **Conclusion:** Our study found that platelet-rich plasma is a safe and effective treatment for knee osteoarthritis, with positive results seen in a six-month observation period.

INTRODUCTION

Platelet-rich plasma (PRP) stands as a biological therapy applied for diverse musculoskeletal injuries entailing tendons, ligaments, cartilage, and bone. This refined substance originates from autologous blood, boasting a platelet concentration surpassing that of whole blood. PRP contains abundant growth factors (GFs) and cytokines scientifically proven to incite cell migration, cell proliferation, angiogenesis, and matrix synthesis, thus fostering the commencement and advancement of the healing process.^[1]

In literature, the abbreviation PRP commonly denotes various preparations comprising plasma, platelets, and growth factors. Variations in the concentration of platelets and bioactive substances within platelet-rich plasma (PRP) are crucial factors influencing its efficacy.^[2,3]

The ideal platelet concentration for PRP remains undetermined, yet a concentration of 10^6 platelets/ μ L within a 5 mL plasma volume is

commonly applied. The role of leukocytes in PRP is not yet fully elucidated, but they might offer certain advantages, such as potential anti-infectious and immune regulatory properties.^[4-6]

Furthermore, leukocytes can aid platelets in stimulating angiogenesis by generating vascular endothelial growth factor (VEGF).^[7]

Platelet-rich plasma finds application in orthopedics across four primary categories:

1. Persistent Tendinopathies
2. Sudden Ligament Injuries
3. Muscle Traumas
4. Ongoing Knee Degeneration – Osteoarthritis

Osteoarthritis (OA) stands as a knee ailment characterized by cartilage degeneration and affliction of neighboring joints. Musculoskeletal discomfort and restricted mobility can result in diminished daily functionality among individuals grappling with osteoarthritis. This deterioration results from an imbalance between cartilage degeneration and regeneration.^[8-11]

The treatment approach for osteoarthritis may involve traditional methods like physical therapy, nonsteroidal anti-inflammatory drugs (NSAIDs), intra-articular glucocorticoid injections, and intra-articular hyaluronan injections. When conservative therapies prove ineffective in managing severe osteoarthritis, joint replacement arthroplasty may be considered.^[12]

Platelet-rich plasma has demonstrated encouraging outcomes in biological regeneration and holds the potential for facilitating the recuperation of osteoarthritis. This therapeutic approach boasts a minimal recurrence rate. Intralesional administration of autologous platelet-rich plasma was employed in a research endeavor to address osteoarthritis.^[13]

MATERIALS AND METHODS

The research titled "Effectiveness of Autologous Platelet-Rich Plasma Injection in Knee Osteoarthritis" was carried out at the Orthopedics Department, focusing on patients visiting the Outpatient Clinic of Varun Arjun Medical College & Rohilkhand Hospital, located in Banthra, Shahjahanpur, Uttar Pradesh.

Study Design: A Randomized, unblinded, and prospective investigation.

Study Setting: Orthopedics Department, Varun Arjun Medical College & Rohilkhand Hospital, situated in Banthra, Shahjahanpur, Uttar Pradesh.

Duration of The Study: From March 2023 to February 2024, spanning a period of 12 months.

Sample Size: A total of 30 individuals presenting symptoms indicative of knee osteoarthritis were included in the study.

Inclusion Criteria

- Individuals diagnosed with clinically confirmed knee osteoarthritis.
- Patients must have experienced symptoms persisting for a minimum of three months.
- Patients must have undergone conservative treatment for at least three months.
- Patients must report pain scores exceeding seven at the time of PRP injection.
- Patients should not have received a local steroid injection within the past 2 months.
- Both genders - males and females.

Exclusion Criteria

- Duration of symptoms less than three months for knee osteoarthritis.
- Pain score below seven.
- Patients who have not attempted conservative treatment.
- Patient who received steroid injection within the past three months.
- Presence of infection or ulceration at the injection site.
- Individuals with secondary osteoarthritis, rheumatoid arthritis, or seronegative spondyloarthritis.
- Pregnant or lactating females.

- Individuals under the age of 18.
- Cases where the diagnosis is uncertain.
- Patients with compromised immune systems.
- Individuals with connective tissue disorders.
- Patients with hemoglobin levels below 10 mg%.
- Patients diagnosed with tumors or metabolic bone diseases.
- Individuals experiencing concurrent back pain.

Prior to administering the PRP injection therapy, we secured informed consent from all patients. We ensured to provide a comprehensive explanation of their medical condition and the specifics of the treatment in a language they understood. Patients were also briefed about the research and its objectives. All participants voluntarily consented to take part in the study and undergo the procedure. To confirm their comprehension and agreement, both the patients and their closest relatives signed the consent document.

The Transfusion Medicine Department at Varun Arjun Medical College & Rohilkhand Hospital in Shahjahanpur, Uttar Pradesh generously agreed to prepare and supply Autologous Platelet Rich Plasma.

Preparation Of PRP

To initiate the process, 20 ml of venous blood is extracted from the cubital vein and transferred into six 2.7 ml vacutainers already containing acid citrate dextrose. These vacutainers, readily accessible in hospitals, should be filled up to their designated markings. Subsequently, the vacutainers are positioned in the centrifuge machine in a balanced manner and spun at 1500 rotations per minute for three minutes. This action separates the blood into two distinct layers, with red blood cells (RBCs) settling at the bottom and plasma, along with platelets, accumulating at the top. Using an 18-gauge needle and syringe, the upper layer is carefully transferred to fresh vacutainers. The newly filled vacutainers are then subjected to centrifugation at 2500 rotations per minute for three minutes. This second spin effectively segregates the plasma into a layer rich in platelets at the bottom and one poor in platelets at the top. Following the removal of the top portion, containing platelet-poor plasma, the platelet-rich plasma is carefully retrieved from the vacutainers, rendering it prepared for use.

The initial platelet count and leukocyte count of the patients were assessed, and the Platelet Rich Plasma was measured to contain eight to ten times the baseline level of platelets.

Injection Protocol: The injection procedure took place in the emergency operating theatre. The patient was positioned supine on the operating table, and the relevant areas were cleaned and covered with sterile drapes. With strict sterile precautions, 2 ml of Platelet-rich plasma was injected into the supra patellar pouch of the knee or the joint cavity, followed by a sterile dressing. The patient was instructed to rest in bed for two days.

Moreover, the patient was advised to abstain from taking NSAIDs for two days prior to and following the injection. In case of fever or discomfort due to pain, Paracetamol could be consumed at a dosage of 500mg. Starting from the second day, the patient was encouraged to resume their regular activities.

Outcome Analysis: Patients were advised to return for follow-up appointments at 6 weeks, 3 months, and 6 months post-injection. The effectiveness of the treatment was assessed by quantifying the decrease in pain, stiffness, and enhancement in physical function utilizing the WOMAC scale. Furthermore, pain reduction was evaluated using the Visual Analog Scale before the injection and at the 6-month mark.

The Womac (Western Ontario And McMaster Universities) Index Of Osteoarthritis

The WOMAC (Western Ontario and McMaster Universities) index is employed for evaluating patients with knee osteoarthritis, encompassing 24 criteria. It serves to track the progression of the condition or ascertain the efficacy of treatment measures.

Severity, on average, during the last 48 hours, of:

Pain

	None	Slight	Moderate	Severe	Extreme
Pain – Walking	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain – Stair climbing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain – Nocturnal	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain – Rest	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pain – Weightbearing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Stiffness:

Morning Stiffness	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Stiffness occurring during the day	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Level of difficulty performing the following functions, on average, during the last 48 hours:

	None	Slight	Moderate	Severe	Extreme
Descending stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ascending stairs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rising from sitting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Standing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Bending to the floor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Walking on flat	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Getting in/out of a car	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Going shopping	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Putting on socks	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rising from bed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Taking of socks	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lying in bed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Getting in/out of bath	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sitting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Getting on/off toilet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Performing heavy domestic duties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Performing light domestic duties	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

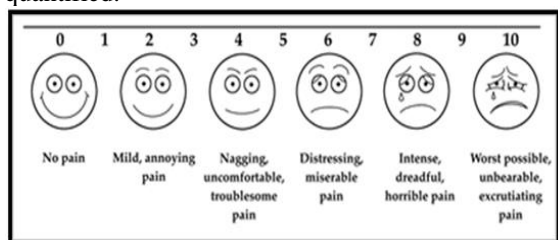
The WOMAC parameters are:

0 – none, 1 – slight, 2 – moderate, 3 – severe, 4 – extreme.

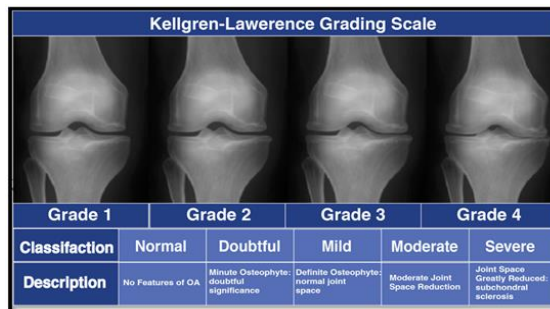
The index is out of a total of 96 possible points, with 0 being the best and 96 being the worst

Visual Analog Scale For Pain

The patient's pain is evaluated using a visual analog scale, where they indicate their pain level and it is quantified.



Kellgren Lawrence Grading Of Osteoarthritis Knee



Ahlback Radiological Criteria

Ahlbäck grade ¹	Anteroposterior stress radiograph	Lateral radiograph
1	Reduction of joint space	
2	Obliteration of joint space	
3	Tibial plateau attrition <5 mm	Posterior part of plateau intact
4	Attrition 5-10 mm	Attrition extends to posterior margin of the plateau
5	Severe subluxation of the tibia	Anterior subluxation of the tibia >10 mm

Synopsis Of Analysis

The research assessed the effectiveness of platelet-rich plasma in treating knee osteoarthritis over a period of one year of follow-up.

Patients underwent a standardized injection procedure and were assessed for pain, stiffness, and physical function before the injection, as well as at 6 weeks, 3 months, and 6 months post-injection for knee osteoarthritis, utilizing the Western Ontario and McMaster Universities Arthritis Index (WOMAC) scale.

To depict the data, descriptive statistics including frequency analysis and percentage analysis were employed for categorical variables, while mean, median, interquartile range (IQR), and standard deviation (SD) were utilized for continuous variables.

To ascertain significant differences in multivariate analysis for repeated measures, Repeated Measures ANOVA was applied with Bonferroni correction to mitigate type I error in multiple comparisons. Similarly, the Friedman test followed by the Wilcoxon signed-rank test was employed for pairwise comparisons.

In all the aforementioned statistical techniques, a significance level of 0.05 was deemed appropriate. The statistical methods utilized for analysis included:

1. Arithmetic Mean
2. Median
3. Interquartile Range (IQR)
4. Standard Deviation (SD)
5. Friedman Test
6. Wilcoxon Signed-Rank Test
7. Analysis of Variance (ANOVA)
8. Bonferroni Correction

The gathered data were inputted into Microsoft Excel 2016 and analyzed using IBM SPSS Statistics

for Windows, Version 29.0. (Armonk, NY: IBM Corp).

RESULTS

This research titled “Efficacy Of Autologous Platelet-Rich Plasma Injection In Knee Osteoarthritis” was conducted at the Orthopedics Department of Varun Arjun Medical College & Rohilkhand Hospital over a period of 12 months. Thirty patients who met the inclusion criteria were recruited for the study. Notably, all 30 patients initially enrolled in the study successfully completed it, with no dropouts observed.

Table 1: Age demographics of Knee Osteoarthritis.

Age demographics		
Age (years)	Frequency	Percent (%)
31 - 40 years	5	16.7
41 - 50 years	7	23.3
51 - 60 years	12	40
61 - 70 years	4	13.3
71 - 80 years	2	6.7
Total	30	100

[Table 1] Age demographics of individuals with knee osteoarthritis indicate that 16.7% fall within the 31-40 years age group, 23.3% in the 41-50 years range, 40.0% in the 51-60 years category, 13.3% in the 61-70 years group, and 6.7% in the 71-80 years bracket.

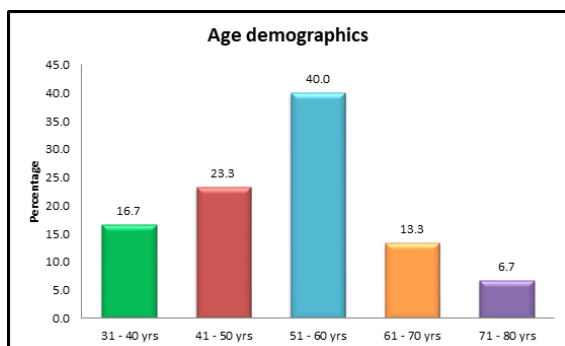


Figure 1: Age Demographics of Knee Osteoarthritis

Table 2: Gender distribution of Knee Osteoarthritis

Gender composition		
SEX	Frequency	Percent (%)
Female	13	43.3
Male	17	56.7
Total	30	100.0

[Table 2] Displays the gender composition within Osteoarthritis cases, with females accounting for 43.3% and males for 56.7% of the total.

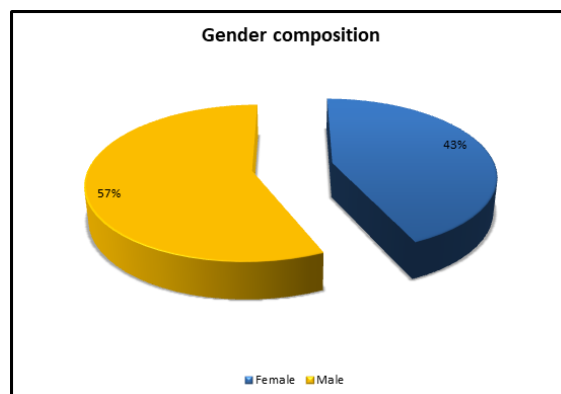


Figure 2: Gender composition Of Knee Osteoarthritis

Table 3: Comparison of Pre injection to 6 months within Womac Score using Repeated measures of ANOVA

Womac Score	Mean	SD	N	F-value	p-value	
Pre injection	72.7	5.0	30	425.906	0.0005**	
6 weeks	60.9	7.4	30			
3 months	46.7	9.3	30			
6 months	34.7	8.8	30			
**Highly statistically significant at a p-value < 0.01 level.						
Pairwise Comparisons						
(I) Womacscore		MD (I-J)	Std. Error	p-value	95% C. I.	
					LB	UB
Pre	6 Weeks	11.733*	.840	0.0005**	9.355	14.112
	3 Months	26.000*	1.325	0.0005**	22.247	29.753
	6 Months	37.933*	1.270	0.0005**	34.336	41.530
6 Weeks	3 Months	14.267*	1.018	0.0005**	11.384	17.150
	6 Months	26.200*	1.288	0.0005**	22.554	29.846
3 Months	6 Months	11.933*	.971	0.0005**	9.185	14.682
**Highly statistically significant at a p-value < 0.01 level.						

[Table 3] Illustrates the comparison of pre-injection to 6 months within the Womac Score utilizing Repeated Measures of ANOVA, yielding an F-value of 425.906 and a p-value of 0.0005, which indicates a high level of statistical significance at $p < 0.01$. Additionally, in pairwise comparisons, the results remain highly statistically significant at the $p < 0.01$ level.

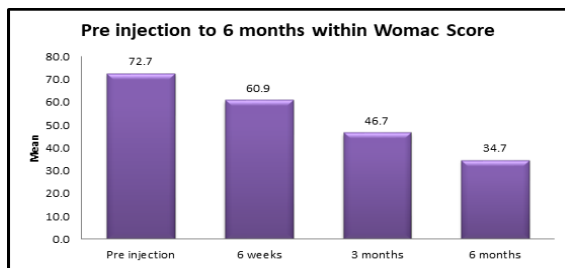


Figure 3: Comparison of Pre injection to 6 months within WOMac Score using Repeated measures of ANOVA

Table 4: Comparison of Pre & Post injection scores within VAS using Wilcoxon Signed Ranks test

VAS	N	Mean	Median	S.D	IQ R	Z-value	p-value
Pre injection score	30	6.80	6.00	1.00	2.00	4.861	0.0005**
Post injection score	30	3.00	2.00	1.31	2.00		

**Highly statistically significant at a p-value < 0.01 level.

[Table 4] Presents the comparison of pre-and post-injection scores within VAS using the Wilcoxon Signed Ranks test, yielding a Z-value of 4.861 and a p-value of 0.0005, indicating a highly significant difference at the $p < 0.01$ level.

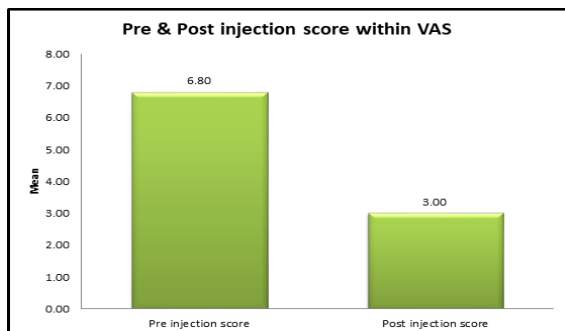


Figure 4: Comparison of Pre & Post injection scores within VAS using Wilcoxon Signed Ranks test

Table 6: Summary statistics for Knee Osteoarthritis.

Summary Statistics					
	N	Minimum	Maximum	Mean	SD
Age	30	32.0	80.0	53.7	11.6
Height	30	142.0	175.0	158.8	7.3
Weight	30	56.0	78.0	67.4	5.9
BMI	30	21.8	32.7	26.8	2.5

[Table 6] Shows the Knee Osteoarthritis Summary Statistics of Age, Height, Weight, and BMI.

DISCUSSION

Platelets contain biologically active substances that aid in blood clotting, such as coagulation factors, adhesive proteins, and protease inhibitors. Additionally, platelets release growth factors like transforming growth factor -beta 1 (TGF- β 1), concentrated growth factor (CGF), VEGF, and platelet-derived growth factor (PDGF), which are

Table 5: Pain relief % distribution of Knee Osteoarthritis

Pain relief %	6th-week followup		3rd-month followup		6th-month followup	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
0 to 25 %	27	90.0	4	13.3	1	3.3
26 - 50 %	3	10.0	24	80.0	9	30.0
51 - 75 %	0	0.0	2	6.7	20	66.7
Total	30	100.0	30	100.0	30	100.0

[Table 5] Shows the distribution of 6th-week follow-up to 6th-month follow-up of Osteoarthritis Pain relief %.

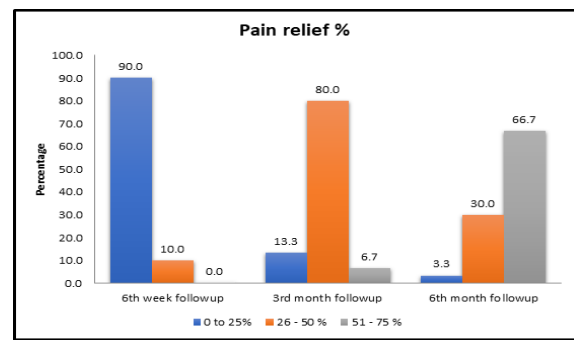


Figure 5: Pain Relief % in Knee Osteoarthritis

activated during platelet activation. These growth factors initiate the tissue healing process by promoting cellular proliferation and differentiation, chemotaxis, tissue debris removal, angiogenesis, and extracellular matrix formation. These tissue healing properties of platelets are used to treat degenerative knee diseases such as osteoarthritis, by locally injecting autologous platelet-rich concentrate.^[14]

Several methods exist for the preparation of autologous platelet-rich plasma, which vary in the duration and speed of centrifugation. The containers used for platelet-rich plasma preparation also differ to minimize the direct handling of blood. Generally, the volume of platelet-rich plasma obtained is around 10 percent of the whole blood used. Alsousou et al used a GPS for the preparation of PRP and collected a PRP volume of approximately 5 ml following 12 minutes of rotations at 3200 rpm. Augustus D et al used a double centrifugation method, which separates blood first into plasma and RBC. The plasma formed was separated again into platelet-rich plasma and platelet-poor plasma by second centrifugation. In this study, we used Augustus D et al's method of double centrifugation and standardized the procedure of preparation of platelet-rich plasma through repeated trial and error.^[15,16]

Platelet-rich plasma, also known as platelet-rich concentrate, autologous platelet gel, or platelet release, is a type of autologous blood that contains a concentration of platelets above the baseline values. The platelet count in our samples ranged from two to six lakhs per cc. Hall MP et al. described that platelet-rich plasma contains a two to eight-fold increase in platelet concentration and a 1-25-fold increase in growth factor concentration. According to Marx RE et al. in the article "What is PRP and what is not PRP?", a concentration of at least 10 lakhs of platelets per ml in five ml of plasma will be associated with enhancement of healing. Alsousou J et al. in a review article described a concentration of five times the normal count as a working definition of PRP.^[15,17,18]

Osteoarthritis is a condition that affects the synovial joints. It is characterized by the focal loss of hyaline cartilage, which leads to the proliferation of new bone and remodelling of joint contour. This happens because there is an imbalance between cartilage regeneration and degeneration. Osteoarthritis is a dynamic repair process of synovial joints that can be triggered by various factors.

We randomly selected 30 patients with classic osteoarthritis symptoms and administered an intra-articular injection of platelet-rich plasma.

The study group's effectiveness of Platelet Rich Plasma in reducing pain, and stiffness, and improving physical function was scored using the WOMAC index. The results were analyzed using Mean, Median, IQR, SD, ANOVA, Friedman Test, and Wilcoxon signed rank test.

In our study distribution of Osteoarthritis by age is as follows: 16.7% for the age group of 31-40 years, 23.3% for 41-50 years, 40.0% for 51-60 years, 13.3% for 61-70 years, and 6.7% for 71-80 years. The gender distribution of Osteoarthritis is 43.3% for females and 56.7% for males.

The pre-injection to 6 months within Womac Score by Repeated Measures of ANOVA had an F-value of 425.906 and a p-value of 0.0005, which shows high statistical significance at $p < 0.01$ level. In

pairwise comparisons, it shows high statistical significance at $p < 0.01$ respectively.

The pre-and post-injection score within VAS by Wilcoxon Signed Ranks test had a Z-value of 4.861 and a p-value of 0.0005, indicating a high statistical significance difference at $p < 0.01$ level.

CONCLUSION

The progression of modernization and improvements in healthcare delivery have significantly increased human lifespan. Consequently, healthcare providers are now focusing on non-communicable and degenerative diseases. Osteoarthritis, characterized by the degeneration of articular cartilage leading to joint failure, has seen substantial advancements in its management over the last century. Depending on the disease stage, treatment options range from conservative approaches such as lifestyle modifications and physiotherapy to surgical interventions like joint replacement arthroplasty.

Researchers are continually exploring molecules that could aid in cartilage regeneration and potentially slow disease progression. One promising avenue is leveraging the beneficial effects of growth factors present in platelets to regenerate cartilage within synovial joints. This method has shown encouraging results.

Our research involved injecting a concentrated platelet mixture into joint cavities and monitoring patients for improvements in pain, stiffness, and physical function. The findings indicated that this treatment consistently alleviated pain and stiffness, significantly enhancing patients' quality of life.

Our study identified an intriguing treatment option for knee osteoarthritis using platelet-rich plasma. The maximum benefit from PRP injection was observed at 2 months and sustained effectiveness for at least 6 months. However, additional trials are necessary to optimize the PRP preparation technique. Overall, the treatment demonstrated efficacy for up to six months.

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