

A Comparative Study on the Effectiveness of Platelet Rich Plasma Injection versus Corticosteroid Injection in Treatment of Adhesive Capsulitis of Shoulder

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Conflict of interest: Nil

Abstract:

Background: The aim of the study was to compare the effects of single intra-articular platelet-rich plasma (PRP) and corticosteroid (CS) injections in patients with adhesive capsulitis of the shoulder.

Design: Patients aged 30–70 years of either sex, diagnosed with adhesive capsulitis of shoulder, with less than 6-month duration, were included. In intra articular corticosteroid (IA-CS, control) group, 30 patients received a single injection (2 ml) of IA-CS and in IA-PRP (test) group, 30 patients received single IA-PRP injection (2 ml) into the glenohumeral joint under ultrasound guidance. All patients were prospectively followed for 24 wks.

Results: Thirty patients in IA-PRP group and thirty in IA-CS group finished the entire 24week study period. At 24 weeks, decrease in QUICK DASH score is observed in IA-PRP group, were 16, compared with 33 in IA-CS group. In range of movement, IA-PRP group showed significant improvement in abduction, internal and external rotations compared with IA-CS group, respectively No major complications were observed in any patients.

Conclusions: At 24week follow-up, a single dose of IA-PRP injection was found to be more effective than an IA-CS injection, in terms of improving pain, disability & shoulder ROM in patients with adhesive capsulitis of the shoulder.

Keywords: Adhesive Capsulitis(AC), Platelet-Rich Plasma(PRP), Corticosteroid(CS), Intra-articular(IA).

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Introduction

One of the common reasons of shoulder pain and upper-extremity impairment is adhesive capsulitis (AC). It interferes with the glenohumeral (GH) joint's abilities, restricting both active and passive shoulder movements¹. The limitation of the shoulder's passive range of motions (ROMs), notably abduction external rotation, has continued to be essential to the clinical diagnosis of AC. In the general population, the prevalence of AC ranges from 2% to 5%, however it can reach 20% in diabetic patients^[1]. Relieving discomfort, restoring movement, and ultimately regaining shoulder function are the objectives of AC treatment. Due to its affordability and patient acceptance, intra-articular corticosteroid (IA-CS) injection is still among the most often used methods of treating AC [1,2]. According to studies, injection of CS into the shoulder joint relieves symptoms and prevents the growth of capsular fibrosis [1,2]. However, it has been discovered that CS injection is linked to hyperglycemia, negative

effects on articular cartilage, an elevated risk of tendon rupture, localised skin depigmentation, and subcutaneous tissue atrophy [3]. Given the potential negative effects of CS injections, it is crucial for both doctors and patients to understand how to create the best treatment plan for patients with AC who are ineligible for or unwilling to receive CS injection. One of the common reasons of shoulder pain and upper-extremity impairment is adhesive capsulitis (AC).

Recent studies have shown that platelet-rich plasma (PRP) injections are beneficial in treating chronic tendon and muscle injuries, tendinopathies, osteoarthritis, and other conditions [4–11]. PRP therapy involves the concentration and subsequent reinjection of autologous "platelets" that were obtained by whole-blood centrifugation. PRP is safe for injection and possesses antinociceptive, anti-inflammatory, and regenerative characteristics, according to studies. With chronic tissue injuries,

platelet-rich plasma can speed up tissue repair while also reducing joint pain and stiffness [5,6,7,8,10,11]. There isn't much proof of its efficacy in AC patients, though.

This study compared the effects of a single IA-PRP injection and a standard single IA-CS injection on pain and shoulder functioning in AC patients. In contrast to IA-CS injection, we believe that reinjecting concentrated platelets may lessen synovial inflammation and speed up the natural repair of the joint capsule, leading to a better reduction in pain and stiffness of the shoulder joint in AC patients.

Methodology (Materials & Methods)

Study Topic: A Comparative Study On The Effectiveness Of Platelet Rich Plasma Injection Versus Corticosteroid Injection In Treatment Of Adhesive Capsulitis Of Shoulder.

Study Venue: Department of Orthopaedics, Tertiary teaching hospital.

Sample Size: Sixty (60).

Study Period: October 2022 to October 2024.

Data Collection: Collection of data as per proforma with prior informed consent from the patients admitted in Orthopaedic ward, Tertiary teaching hospital.

Inclusion Criteria:

- Patients above 30 years of age of both gender,
- Pain for less than 12 months,
- Limitations of both active & passive movements of glenohumeral joint of $\geq 25\%$ in at least 2 directions (abduction, external rotation, internal rotation & flexion), as compared with the contralateral shoulder in the scapular plane

and in progressive degree of horizontal adduction.

Exclusion Criteria:

- Patients with Concurrent bilateral shoulder pain
- Uncontrolled Diabetes mellitus.
- Overt hypothyroidism or hyperthyroidism,
- Patients who received any drug by intra-articular injection for treatment within 6 months prior to the enrolment.
- History of shoulder trauma including dislocation- subluxation & Fracture.
- History of breast cancer- or surgery around shoulder- neck and upper Back.
- Neurological deficit.
- History of previous adverse reactions to corticosteroids.
- Secondary adhesive capsulitis, Systemic inflammatory disease including rheumatoid arthritis, MRI evidence of rotator cuff injury.

Study Design

A prospective cohort research was conducted here. Figure 1 displays a schematic diagram of the study. 60 AC patients were enrolled in the current study after giving their informed consent. In the test group (IA- PRP group), 30 patients received a single (2 ml) IA-PRP injection into the GH joint, whereas the control group (IA-CS group) had a single (2 ml) CS injection. PRP was administered to individuals with DM or a history of CS side effects, while CS injection was given to others. To create 2 ml of CS injection, 1 ml (40 mg) of Triamcinolone acetonide and 1 ml 2% lignocaine were combined.

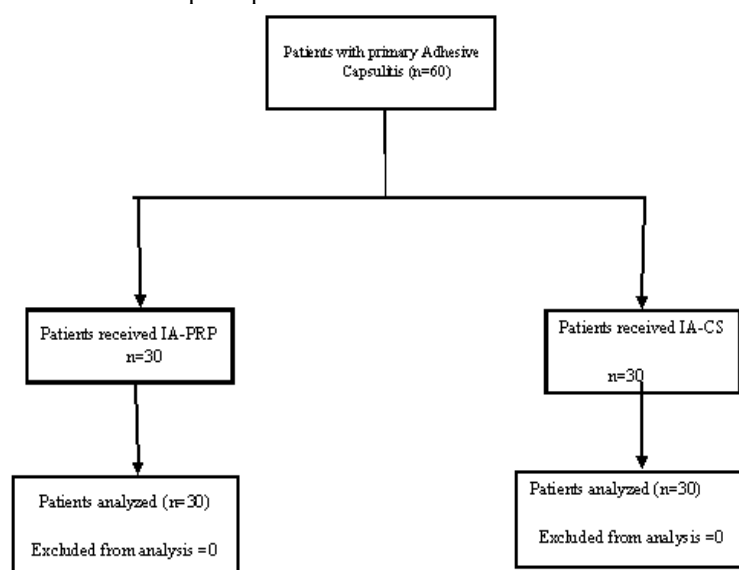


Figure 1: Flow diagram indicating the progress of participants through the study

Injection protocol: Platelet rich plasma and Steroid groups were created alternately for patients who met the inclusion criteria. After describing the study, the advantages and drawbacks of the intervention, and the requirement for regular follow-up, the patient's consent was acquired. Patients in the platelet-rich plasma (PRP) group had fresh blood collected from them (approximately 28 ml), and anticoagulant was then added (2ml). Then, 2 ml of PRP was generated by centrifuging the blood at 2500 and 3500 rpm for roughly ten and fifteen minutes, respectively. Scores before and after the injection were computed.

Injection technique: A transducer was used by an interventional radiologist to administer each and every shot. Both intervention groups used the posterior route for intra articular injection into the Glenohumeral joint^[12,13]. The patients were seated on a chair with their hands on their thighs in an upright position. The Glenohumeral joint was reached by inserting a 20-gauge needle semi-obliquely and parallel to the ultrasound probe. While injecting the fluid (CS or PRP), the articular capsule's expansion was monitored. All intra-articular injections were administered in an aseptic manner.

Post injection protocol: The patients were directed to avoid doing overhead motion and rotatory shoulder movements for the first two days. After the treatment, patients received detailed instructions for a home exercise programme for improving range of motion (ROM), which included wall-climbing exercises, the Codman ^[14]and pendulum stretches for the shoulders, as well as stretches for the posterior and inferior shoulders. The exercises have to be done twice daily for thirty minutes starting two days following the injection. For the duration of the twelve-week observation period, NSAIDs were not allowed. For extreme pain or discomfort, patients were allowed to take up to 1300 mg of acetaminophen (650 mg) each day in the form of oral pills. Before their follow-up consultation, all patients were instructed to stop taking their prescriptions 48 hours in advance. Patients were strongly recommended to maintain a notebook for their workouts, where they could record their frequency, duration, and any challenges, as well as records of when they obtained tablets. The notebooks were examined at each subsequent session. Additionally, patients were contacted to remind them not to get any additional medicine or physical agents and to motivate them to keep exercising.

QuickDASH

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Do heavy household chores (e.g., wash walls, floors).	1	2	3	4	5
3. Carry a shopping bag or briefcase.	1	2	3	4	5
4. Wash your back.	1	2	3	4	5
5. Use a knife to cut food.	1	2	3	4	5
6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
7. During the past week, to what extent has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. (circle number)

	NONE	MILD	MODERATE	SEVERE	EXTREME
9. Arm, shoulder or hand pain.	1	2	3	4	5
10. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? (circle number)	1	2	3	4	5

QuickDASH DISABILITY/SYMP TOM SCORE = $\left(\frac{\text{sum of } n \text{ responses}}{n} \right) \cdot 1 \times 25$, where n is equal to the number of completed responses.

A QuickDASH score may not be calculated if there is greater than 1 missing item.

Figure 2: Quick DASH SCORE

Outcome Measures: A self-report questionnaire is used to assess the patient's clinical outcome at each review interval. A quick version of Disabilities of the Arm, Shoulder, and Hand is used to evaluate the severity of adhesive capsulitis prior to injection (Quick DASH) in Figure 2. Baseline characteristics were collected from all patients. Follow-up on the condition's outcome is performed utilising the same score at 4, 8, 12 and 24 weeks after the administration of either single dose of Platelet Rich Plasma injection or single dose of Corticosteroid injection, and will be examined with the aid of predesigned proforma.

Statistical Analysis: The needed patient count was determined using a power analysis software. The sample size was calculated with Quick DASH as the major outcome measure. (Pooled standard deviation = 14, two-sided t test = 0.05) This study was planned to have 80% power to detect a difference of 10 points improvement in Quick DASH scoring between the two groups. Each group need 30 volunteers to do this. The SPSS programme (Statistical Package of Social Sciences, Chicago, IL) Version 22.0 was used to conduct the statistical analyses. Continuous data are displayed as mean SD, and categorical data are expressed as a

percentage or a proportion. By using repeated-measure analysis of variance, the differences in the changes of all parameters at various time periods were compared. To compare the changes in various parameters from the baseline to the second, third, fourth, and fifth visits, multivariate repeated ANOVA test was performed. In all tests, a P value of 0.05 or lower was regarded as statistically significant.

Results

Clinical Characteristics of the Patients: Sixty subjects were recruited in this study. Patients 60 cases with adhesive capsulitis within the aforementioned time frame that matched the required criteria were included in the study. Total 33 males with 20 right-sided adhesive capsulitis & 13 left-sided adhesive capsulitis and 27 females with 15 right-sided adhesive capsulitis & 12 left-sided adhesive capsulitis. With a range of 30 to 67 years, the average age was 43.4 years. The typical time of the symptoms was 7.5 months.

All the relevant data were analysed. The average QUICK DASH SCORE in both the groups of pre-injection, 4 weeks, 8 weeks, 12 weeks, and 24 weeks post-injection are shown in the below table.

Table 1: quick dash score comparison between prp and steroid groups

Follow-up	QUICK DASH SCORE (PRP group)	QUICK DASH SCORE (Steroid group)
Pre-inj.	84	86
Post inj. 4 weeks	64	65
Post inj. 8 weeks	42	47
Post inj. 12 weeks	24	36
Post inj. 24 weeks	16	33

From the below curves, it is clear that the steroid group had a steep curve than the PRP group indicating the faster relief of pain initially. But by the end of the 24 weeks follow up the steroid group shows a flat curve pattern whereas the platelet-rich plasma group shows a falling curve pattern.

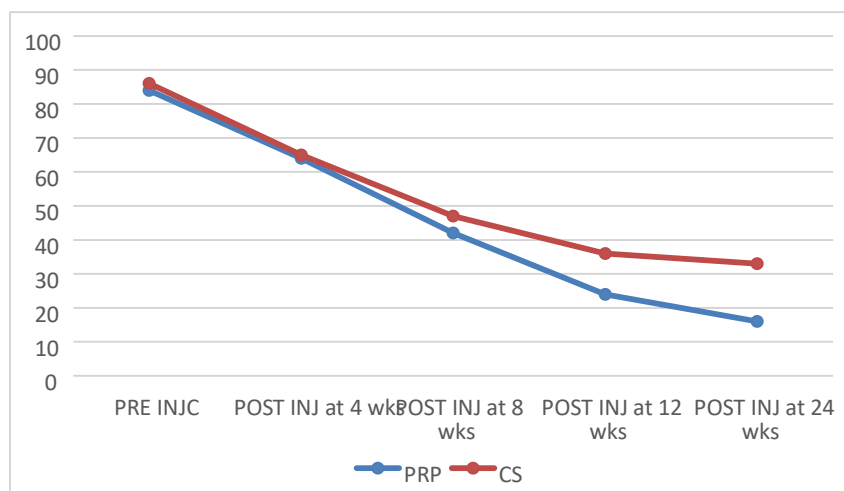


Figure 3: Quick dash comparison between prp and steroid group

In this study, the QUICK DASH score in the platelet-rich plasma group is decreased from 84 to 16 at 24 weeks, when compared to the pre-injection score. Whereas the QUICK DASH score in the steroid group is decreased from 86 to 33 at 24 weeks, when compared to the pre-injection score.

Paired Sample Statistics of Prp Group:

Table 2: comparison between quick dash score means of pre- injection and 4,8,12,24 weeks respectively in prp group only

		N	Mean	Std. Deviation	Mean differences	Standard deviation of mean differences	P value
Pair 1	PRE INJ	30	83.83	6.968	19.867	0.730	0.003
	Week 4	30	63.97	6.891			
Pair 2	PRE INJ	30	83.83	6.968	41.800	0.805	<0.001
	Week 8	30	42.03	6.790			
Pair 3	PRE INJ	30	83.83	6.968	59.933	1.112	<0.001
	Week 12	30	23.90	6.789			
Pair 4	PRE INJ	30	83.83	6.968	67.933	1.112	<0.001
	Week 24	30	15.90	6.789			

Results in Paired sample test (p value) in PRP group between PRE INJ and POST INJ 4,8,12,24 WEEKS Quick DASH scores respectively gave a strong significance. According to these statistical reports, the patient Quick DASH scores are decreasing gradually, when Platelet rich plasma is given.

Paired Sample Statistics of Cs Group:

Table 3: Comparison between quick dash score means of pre-injection and 4,8,12,24 weeks respectively in cs group only

		N	Mean	Std. Deviation	Mean differences	Standard Deviation of Mean Differences	P Value
Pair 1	PRE INJ	30	86.17	6.613	20.900	0.305	0.004
	Week 4	30	65.27	6.560			
Pair 2	PRE INJ	30	86.17	6.613	39.033	0.615	0.003
	Week 8	30	47.13	6.522			
Pair 3	PRE INJ	30	86.17	6.613	50.300	1.860	<0.001
	Week 12	30	35.87	6.684			
Pair 4	PRE INJ	30	86.17	6.613	54.267	3.290	<0.001
	Week 24	30	31.90	6.472			

Results in Paired sample test (p value) in CS group between PRE INJ and POST INJ 4,8,12,24 WEEKS Quick DASH scores respectively gave a strong significance. According to these statistical reports, the patient Quick DASH scores are decreasing gradually, when Corticosteroid is given.

Table 4: Paired sample tests between prp & cs groups

Group Statistics				
	Group	N	Mean	Standard Deviation
Preinjection	PRP	30	83.83	6.968
	CS	30	86.17	6.613
4 Weeks	PRP	30	63.97	6.891
	CS	30	65.27	6.560
8 Weeks	PRP	30	42.03	6.790
	CS	30	47.13	6.522
12 Weeks	PRP	30	23.90	6.789
	CS	30	35.87	6.684
24 Weeks	PRP	30	15.90	6.789
	CS	30	31.90	6.472

Table 5: T test between prp & cs group in respective weeks

T Test for Quality of Means		P Values
Pre-Injection	Equal variances assumed	0.189
4 Weeks	Equal variances assumed	0.457
8 Weeks	Equal variances assumed	0.004
12 Weeks	Equal variances assumed	<0.001
24 Weeks	Equal variances assumed	<0.001

For the Comparison between the Quick DASH Scores of PRP and CS patient groups, Statistical T test is done. The P value is insignificant at 4th week. Later it became more significant at 24th week.

Table 6: Multivariate repeated anova test

Multivariate ANOVA Tests		
Effect		P Value
Factor 1	Pillai's Trace	<0.001
	Wilks' Lambda	<0.001
	Hotelling's Trace	<0.001
	Roy's Largest Root	<0.001
	Mauchly's Test of Sphericity	<0.001

Discussion

P value Results from pre and post injections of 4,8,12,24 weeks came out that both Platelet rich plasma & Corticosteroids are useful in improving the R.O.M and pain relief in period of 6 months. But after doing Comparative T test study, the statistics in 4th week states that corticosteroids are

giving good pain relief and R.O.M improvement (p value – 0.457). Later on, after continuous follow up of 8,12,24 weeks, greater improvement is seen in patients treated with PRP than CS (p value <0.001). Multi-variate repeated ANOVA Tests of different factors also have p value<0.001 which indicates strong significance of the study.

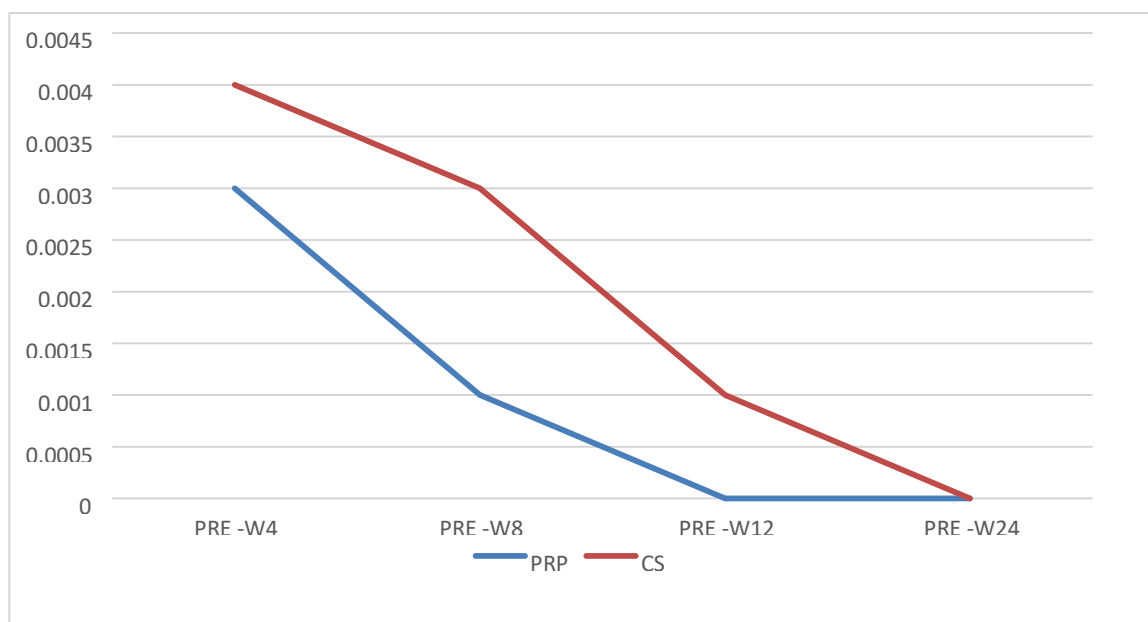


Figure 4: Line diagram of p values of prp & cs groups

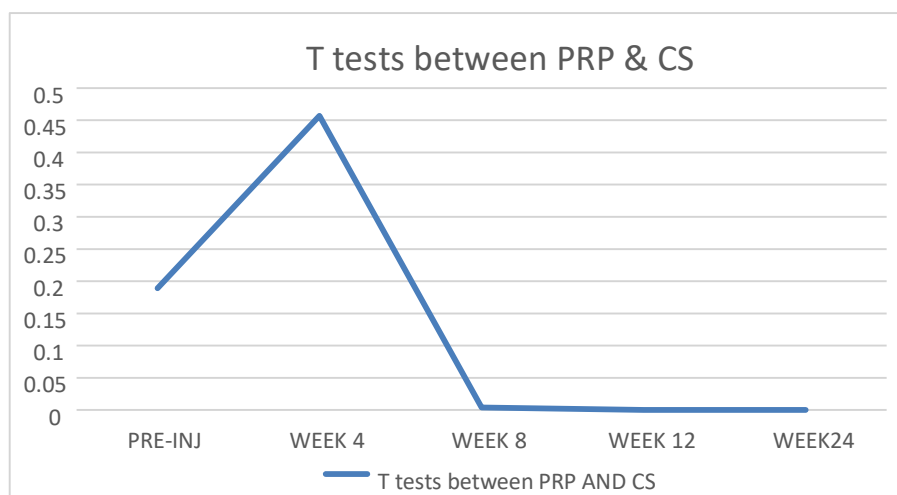


Figure 5: T test between prp & cs groups

There by comparing the efficacy of PRP & CS injections in the treatment of Adhesive Capsulitis, at 24weeks intra-articular PRP injection provided good pain relief and better functional improvement than Corticosteroid injection. The intra-articular PRP group improved shoulder ROM significantly as well. Both groups experienced a significant reduction in pain within the first four weeks of intervention. At 4th week, Corticosteroid group is more statistically significant. But at the end of 24 weeks, the PRP group showed significant improvement in Quick DASH score. Patients in the PRP group consumed less acetaminophen, which indirectly confirmed that the PRP group experienced better pain relief than the CS groups. Patients who received PRP injections reported higher levels of treatment satisfaction.

In 2017 Shashank Yeshwanth Kothari et al observed similar trend in 190 patients, by giving a single dose of PRP injection resulted in significant improvement in shoulder R.O.M, pain & function ultrasonic therapy in 190 patients with A.C shoulder [15]. In 2018, Dalia Salah Saif et al reported that intra-articular injections with both PRP and steroids are effective, non-surgically less invasive, and cost effective lines of treatment for mild-moderate shoulder osteoarthritis, with superiority to PRP in terms of long-term therapeutic effects compared to steroid injection [27]. In 2019, Havva Talay calş et al. proposed that PRP provides analgesia through its effects on cannabinoid receptors, in addition to a complex and unexplained mechanism of action associated with enriched growth factor content and a protein in platelet alpha granules, which initially induces a proinflammatory mechanism and then decreases inflammation and helps in treating adhesive capsulitis. In 2021, Apurba Barman et al reported that PRP injections significantly improved shoulder pain & function in a diabetic population when

compared to an institution-based physical training programme for shoulder AC [17].

The study's advantages included a clear definition of the conditions, enrollment of the entire population with adhesive capsulitis, ultrasound-guided injections, and analysis of functional outcomes at different time points. These factors all provided top-notch proof of the efficacy of PRP and CS injections as well as their effects over time. Patients enrolled from different groups had similar baseline characteristics; no statistically significant differences were discovered between study populations. All trial participants received intra-articular injections that were guided by ultrasonography. All of the treatments were carried out by a single operator who has experience providing ultrasound-guided intraarticular injections. Using capsular distension during the injection, the accuracy of an ultrasound-guided injection was assessed in real time.

Adhesive capsulitis is postulated to be an inflammatory and fibrotic condition. Corticosteroid injections have demonstrated an outcome for Adhesive capsulitis by reducing inflammation, which has resulted in improved clinical outcome [18]. PRP's detailed mechanism of action, on the other hand, is not well understood because it has both pro-inflammatory & anti-inflammatory properties. According to literature, PRP releases a variety of growth factors like platelet derived growth factor, transforming growth factor, vascular & epidermal endothelial growth factor [19,20,21], that are essential for tissue repair mechanism, but also a high amount of RANTES/ CCL5 (major monocyte chemo attractant factor) from its alpha granules [22]. RANTES/CCL5 is a C-C chemokine subfamily member that regulates leukocyte recruitment and diminishes inflammatory & nociceptive responses. RANTES/ CCL5 hinders the production of many cytokines by basophils and lowers concentration of A4 lipoxin (anti-

inflammatory marker), reducing the count of inflammatory cells. Aside from that, Platelet rich plasma produces hepatocyte growth factor & tumour necrosis factor, both of which have potent anti-inflammatory properties [23]. PRP's anti nociceptive effect probably due to cannabinoid receptor augmentation, specifically CB1 and CB2 [24].

Platelets concentration in platelet rich plasma primarily determines PRP quality [20]. Because more platelets in PRP can result in a more significant clinical response [25]. Our method yielded a Mean Platelet count of $696 \times 10^3/l$. We obtained a greater than four times increase in the number of platelets in PRP, which was previously considered a standard and effective count. Leucocytes presence in PRP and their impact on the clinical effectiveness of platelets are highly controversial. Leucocytes can trigger an inflammatory response, and while some studies have advised against using them in PRP because of this, others also have indicated that leucocytes have positive effects like antimicrobial and immunological resistance [26,27]. As previously stated, PRP was prepared in this study using a double centrifugation technique. Our PRP product's mean leucocyte concentration, which ranged from 0.1 to $1.5 \times 10^3/l$, was thus far lower than that of the standardised leucocyte reduced blood product [28].

The fact that PRP may have significant benefits on all stages of tissue healing, including the inflammatory, proliferative & remodelling phases of capsular repair in Adhesive Capsulitis, may help to explain why PRP patients in our study experienced greater improvements. PRP most likely altered synovial fluid cytokine levels and decreased synovial membrane hyperplasia more efficiently than CS, leading to improved shoulder pain alleviation. Patients may have performed home exercises more properly, leading to a temporary improvement in overall clinical outcome, because pain dropped dramatically and overall joint. These explanations are based on scientifically informed suspicions rather than data from this study, which did not investigate the molecular basis of PRP's action on capsular healing. More research is needed, however, to confirm the findings and understand the detailed mechanisms by which PRP works, as well as to determine whether the improvement is only temporary or if PRP plays a more important role through disease-modifying properties.

When the results of this study are compared to the results of six-month follow-up, the result for the CS group is reduced. whereas the PRP group's outcome is preserved. The platelet-rich plasma group had higher pre-injection Quick DASH scores and lower after 24 weeks, which was a significant

finding. This adds to our belief that platelet-rich plasma injection is superior to corticosteroid injection.

Uniform administration of PRP and corticosteroids in alternative patients, Small sample size are Limitations for this study. Proper randomisation of the patient groups, Use of large sample size, Increase of follow-up period are the recommendations for further studies.

Conclusion

In conclusion, the comparative study of management of adhesive capsulitis with platelet-rich plasma vs corticosteroid injection shows that a single dose of Platelet-rich plasma injection improves shoulder pain and functional activities more efficiently than injecting single dose Corticosteroid into the Adhesive Capsulitis. These improvements were maintained over in our follow-up period without any significant complications.

Corticosteroid gives better results up to the Fourth week and after that, the effect decreased slightly. Long-term follow-up with a larger number of patients is required to assess the long-term benefits of pain relief & functional improvement in adhesive capsulitis.

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