International Journal of Research in Orthopaedics
Avhad TA et al. Int J Res Orthop. 2024 Jul;10(4):769-775
http://www.ijoro.org

Original Research Article

DOI: https://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20241610

Comparison of clinical and functional outcomes of physical therapy alone versus additional intraarticular injection of platelet rich plasma in treatment of frozen shoulder in Indian population

Tanmay A. Avhad*, Sahil Lombar, Neeraj Kalra

Department of Orthopaedics, TNMC and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India

Received: 25 May 2024
Revised: 31 May 2024
Accepted: 04 June 2024

***Correspondence:**
Dr. Tanmay A. Avhad,
E-mail: tanmayavhad@gmail.com

ABSTRACT

Background: Frozen shoulder (adhesive capsulitis) involves significant restriction of shoulder motion due to an inflammatory process and typically follows stages of pain, stiffness, and recovery over 2-3 years. This study explores the efficacy of platelet-rich plasma (PRP) injections, alongside conventional physiotherapy, as a non-operative treatment to enhance recovery in patients with adhesive capsulitis.
Methods: This prospective, randomized, open, blinded, single-center clinical study involving 50 patients with adhesive capsulitis, comparing intra-articular PRP injections and physical therapy with physical therapy alone over 24 weeks. Primary outcomes were assessed using the shoulder pain and disability index (SPADI) and visual analog scale (VAS), with follow-ups at 6, 12, and 24 weeks to evaluate pain, function, and patient satisfaction.
Results: In adhesive capsulitis (AC), intra-articular platelet-rich plasma (IA-PRP) injections with physical therapy (PT) provided superior pain relief, functional improvement, and higher treatment satisfaction after 24 weeks compared to PT alone. The IA-PRP group also showed better VAS scores and reduced acetaminophen use, indicating more effective pain management.
Conclusions: In AC, IA-PRP injections showed greater pain relief and improved shoulder mobility compared to PT alone after 12 weeks. PRP's effectiveness highlights its potential, especially when corticosteroids are unsuitable, though longer-term studies are needed to confirm these results.

Keywords: Platelet rich plasma, Adhesive capsulitis, Frozen shoulder, Intra-articular steroid, Physical therapy

INTRODUCTION

Frozen shoulder (FS), also known as adhesive capsulitis, is defined as "a condition of uncertain etiology, characterized by significant restriction of both active and passive shoulder motion that occurs in the absence of a known intrinsic shoulder disorder".[1] FS is a prevalent source of shoulder discomfort and impairment, impacting around 2% to 4% of the overall population. The highest occurrence of FS is typically observed in individuals aged between their fifth and sixth decades, with a slightly higher prevalence in women compared to men.[2] The widely acknowledged hypothesis involves an inflammatory sequence that results in the contraction of the front-upper capsule, the rotator interval, and the coracohumeral ligaments within the shoulder joint. These processes contribute to the characteristic reduction in passive external rotation observed in FS.[3]

The majority of cases exhibit a gratifying recovery, although the process may extend over a period of 2 to 3 years. This investigation explores the circumstances under which adhesive capsulitis should be included in the list of potential diagnoses and outlines appropriate evaluation methods. Furthermore, it emphasizes the significance of the interprofessional team's involvement in the care of

individuals affected by this condition.[4] Traditionally, FS has been characterized as a self-limiting condition with distinct stages: freezing, frozen, and thawing. Nevertheless, establishing a precise demarcation between these stages proves challenging in the absence of clear-cut criteria. Instead, a more fitting perspective acknowledges a continuous spectrum of the condition.[5] Restriction and discomfort manifest during both passive and active assessments, distinguishing it from rotator cuff disease, where passive movements traditionally exhibit a complete range.[6] Another distinguishing factor is the presence of shoulder crepitus, which is more indicative of arthritis.[7]

Typically, less invasive treatments are initially explored, but there's a growing trend toward earlier consideration of more invasive interventions, particularly surgical capsular release. However, uncertainties persist regarding the optimal timing for such interventions and their clinical and cost effectiveness.[8]

Various treatment options have been described for managing frozen shoulder such as, oral analgesia, physiotherapy, intraarticular platelet rich plasma therapy, hydrotherapy, intraarticular steroid injections, and surgical release.[9]

Although three phases are delineated (pain, stiffness, and resolution), they frequently overlap. Patients may present with either a "pain-predominant" or "stiffness-predominant" FS.

FS commonly advances through three distinct stages: freezing (painful), frozen (adhesive), and thawing. The freezing stage, lasting approximately 2–9 months, is characterized by a gradual onset of widespread, intense shoulder pain that typically intensifies during nighttime. As the frozen stage ensues, there is a distinctive progressive loss of glenohumeral flexion, abduction, internal rotation, and external rotation, accompanied by a subsiding of pain. This stage can persist for 4–12 months. Finally, in the thawing stage, patients undergo a gradual restoration of range of motion, a process that spans about 5–26 months for completion.[10]

Effect of physiotherapy for managing frozen shoulder has well been demonstrated in the past and stands as a pillar in managing the condition. Platelet-rich plasma (PRP) is an autologous concentration of human platelets within a small volume of plasma. The process of producing PRP through centrifugation has been streamlined, making it applicable in both office settings, outpatient procedures and operating rooms.[11] PRP has the capacity to stimulate collagen and growth factor production, potentially increasing the presence of stem cells which enhances the healing process by delivering elevated concentrations of alpha-granules containing biologically active substances, such as vascular endothelial growth factor and transforming growth factor-β, to areas of soft tissue damage.[12]

Our study was motivated by the need to investigate the role of PRP in our local population, especially given the absence of available data on its use in adhesive capsulitis. PRP has found extensive application in various orthopedic conditions, making it a promising non-operative treatment option that could potentially alleviate the burden on hospitals and mitigate the risk of limb disability and its effects when used along with conventional physiotherapy as an adjunct to mitigate this condition

Objectives

This study aims to compare the clinical and functional outcomes of treating frozen shoulder in the Indian population using physical therapy alone versus physical therapy combined with intraarticular PRP injections. It focuses on evaluating improvements in the active and passive range of motion at the shoulder, assessing pain reduction using standardized scales and indices, and exploring any demographic associations with treatment efficacy. Additionally, the study seeks to measure patient satisfaction at the conclusion of the treatment using a Likert scale to determine the overall effectiveness and patient perception of each treatment approach.

METHODS

Trial design

This study was a parallel-group, prospective, randomized, open, blinded), single-center clinical study. There was central randomization, and the person doing randomization was not part of the study. Patients were recruited to different treatment regimens following proper randomization. The trial was conducted according to the principles of the consolidated standards of reporting trials (CONSORT).

Site of the study

The study will be conducted from December 2023 to May 2024 at the Department of Orthopedics, Topiwala National Medical College and B.Y.L Nair Charitable Hospital, Mumbai, Maharashtra, India.

Participants

After receiving the approval from the institutional ethics board committee for the study, as per Barman et al.[13] A total sample size of 50 patients from the outpatient department (OPD), department of orthopedics, TNMC and BYL Nair hospital were selected who were clinically diagnosed to have frozen shoulder and willing to participate were randomized into two groups. A written informed consent regarding participation was obtained before recruitment. The complete procedure of the study was explained to all participants in their language by the investigator before recruitment.

Inclusion criteria

Patient with pain and stiffness in the affected shoulder for more than three months without any preceding trauma. The pain should be rated at six or higher on a visual analogue scale (VAS). There must be a restriction in the passive range of motion (ROM) of the shoulder joint by more than 30° in external rotation and at least one other direction (either abduction or forward flexion). Additionally, patients should have a normal anteroposterior radiograph of the glenohumeral joint in neutral rotation and be over 18 years old.

Exclusion criteria

History of any prior surgery to the shoulder, systemic inflammatory diseases, neurological disorders affecting the upper limb, significant trauma within the last three months, hematological disorders, or current use of antiplatelet or anticoagulant therapy. Patients unwilling to participate, those with a history of shoulder injection within the past six months, and pregnant or breastfeeding females will also be excluded from the study.

With assistance of department of pathology for procuring the processing the PRP, one of the groups was administered 2 ml autologous PRP. To prepare PRP, about 15 ml of the patient's blood was drawn through a scalp vein catheter. The PRP was prepared using a differential centrifugation technique with two spins. The blood was collected in three citrate tubes having 0.9% sodium citrate as an anticoagulant. The first spin was performed at 1,500 rpm for 15 minutes using a laboratory centrifuge. The upper half of the supernatant was discarded. The lower halves of the supernatant from all three tubes were transferred into another plain tube for the second spin. The second spin was performed at 2,500 rpm for 10 minutes. The upper half of the supernatant was discarded. Three milliliters of the lower half were taken into a syringe having 0.1 mL of calcium chloride. At the end of the preparation of PRP was used for ultrasound guided intra-articular injection within 30 minutes of preparation for optimum effect in association with the department of radiology at BYL Nair hospital.[14]

All patients were advised regarding post-injection care. The possibility of pain increasing during the initial two weeks was explained to the patient. Post-injection, patients were prescribed paracetamol (500 mg twice a day orally for three days) for pain relief in both groups. Patients were advised to rest during the initial two weeks and avoid strenuous activities by the extremity under study after the injection. Physiotherapy regime and protocol by certified physiotherapists at the institution was incorporated for both the groups in the form of range of motion exercises for the shoulder with passive mobilization techniques mobilizations to augment scapulothoracic movement, active and auto-assisted stretching techniques was incorporated twice a day for 3 months.

Assessment and follow-up

Upon enrollment in the study, demographic information, baseline clinical observations, pain duration, affected side dominancy, and any associated comorbidities were systematically recorded. Relevant X-ray findings were also documented, and special investigations were conducted based on the identified comorbidities in each case. Follow-up assessments were scheduled at the 6th, 12th, and 24th weeks for all patients in both groups.

Pain and functional evaluations, utilizing the VAS and the shoulder pain and disability index (SPADI), respectively, were performed at each follow-up. Any adverse effects were diligently observed, documented, and reported. All collected data at 24 weeks were meticulously recorded in a designated case report form (CRF) tailored for the project and further organized in Excel sheets for comprehensive analysis.

Outcome measures

The primary outcome measure in this study was the SPADI and VAS at the 24 -week follow-up.[15] The SPADI comprises 13 questions divided into two domains: pain and disability. Responses to items were rated on an eleven-point scale (0-10), resulting in a score ranging from 0 (indicating the best) to 100 (indicating the worst). Passive range of motion (ROM) was assessed with a goniometer and patient satisfaction regarding changes in pain and function was gauged using a five-point Likert scale ("worse," "unchanged," "unsatisfactory improved," "satisfactory improved," and "good to very good improved").

Statistical analysis

Data was entered into Microsoft excel (Windows 7; Version 2007) and analyses were done using the statistical package for social sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical variables were determined. Association between variables was analyzed by using Chi-square test for categorical variables. Unpaired t test was used to compare mean of quantitative variables between cases and controls. Bar charts and pie charts were used for visual representation of the analyzed data. Level of significance was set at 0.05.

RESULTS

Our 50-patient cohort, patients were categorized in two groups of 25 each, A and B with patients of adhesive capsulitis managed with intraarticular injection of PRP along with concomitant physical therapy (group A) and patients given only physical therapy (group B) and results are as followed by independent t test, chi square test.

Comparison of age between study groups (n=50)

Distribution of age (years) was comparable between group A and B (31-40 years: 20% versus 24% respectively, 41-50 years: 44% versus 28% respectively, 51-60 years: 28% versus 28% and >60 years: 8% versus 20% respectively).

Mean±SD of age (years) in group A was 46.96±8.59 and in group B was 49.84±12.46 with no significant difference between them. (p value=0.519) by Chi-square test (Figure 1).

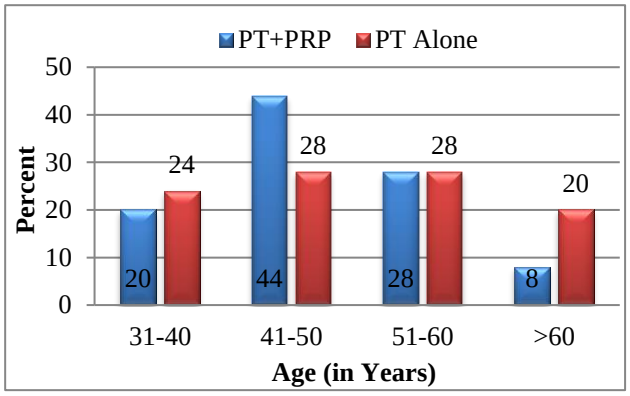

Figure 1: Comparison of age between study groups (n=50).

Comparison of gender between study groups (n=50)

Distribution of gender was comparable between group A and B (female: 56% versus 60% respectively, male: 44% versus 40% respectively) (p value=0.058) with no significance between them (p value=0.774) by Chi-square test (Figure 2).

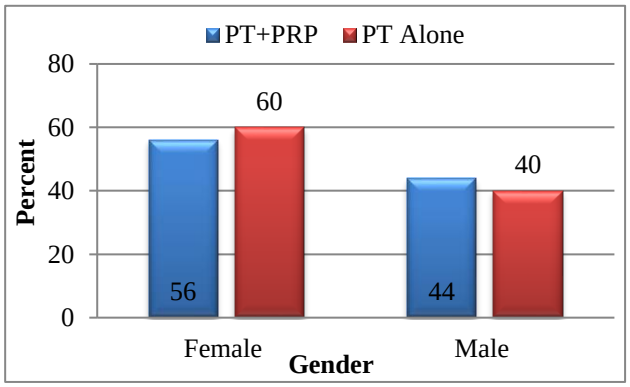

Figure 2: Comparison of gender between study groups (n=50).

Comparison of SPADI pain score at 24 weeks between study groups (n=50)

SPADI pain score was significantly lower in group A as compared to group B.

Mean±SD of total SPADI pain score in group A was 20.92±3.98 which was significantly lower as compared to group B (24.96±4.73) (p value=0.002) by unpaired t test (Figure 3).

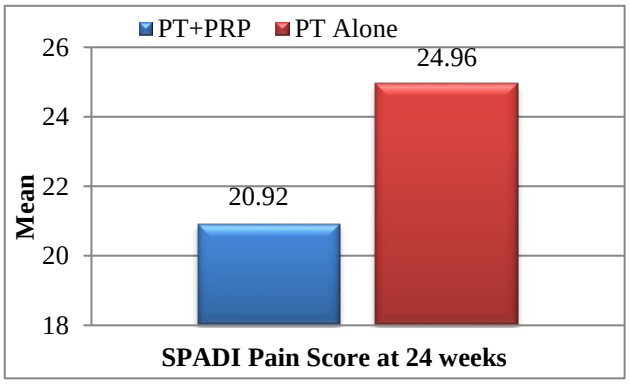

Figure 3: Comparison of SPADI pain score at 24 weeks between study groups (n=50).

Comparison of SPADI disability score at 24 weeks between study groups (n=50)

SPADI disability score was significantly lower in group A as compared to group B.

Mean±SD of total SPADI disability score in group A was 23.52±3.19 which was significantly lower as compared to group B (29.08±3.59) (p value≤0.001) by unpaired t test (Figure 4).

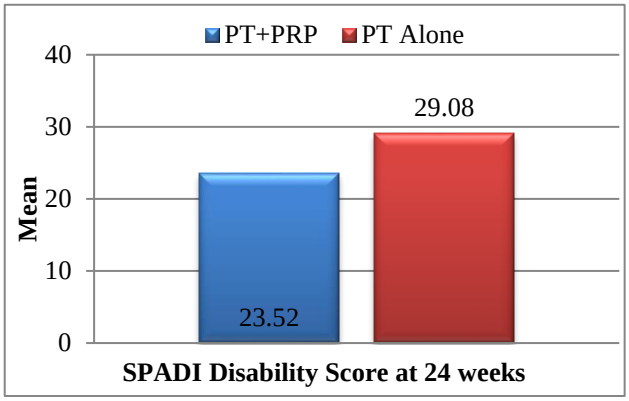

Figure 4: Comparison of SPADI disability score at 24 weeks between study groups (n=50).

Comparison of VAS score at 8 weeks between study groups (n=50)

VAS score was significantly lower in group A as compared to group B.

Mean±SD of VAS score in group A was 4.16±1.10 which was significantly lower as compared to group B (5.04±1.33) (p value=0.015) by unpaired t test (Table 1).

Table 1: Comparison of VAS score at 8 weeks between study groups (n=50).

VAS score	Group, mean (SD)	
	PT+PRP (n=25)	PT alone (n=25)
Values	4.16 (1.10)	5.04 (1.33)

Unpaired t test, p value=0.015, significant.

Comparison of range of motion (abduction) between study groups (n=50)

Abduction was significantly higher in group A as compared to group B.

Mean±SD of Abduction in group A was 103.60±3.14.39 which was significantly higher as compared to group B (93.20±14.64) (p value=0.015) by unpaired t test (Table 2).

Table 2: Comparison of range of motion between study groups (n=50).

Abduction	Group, mean (SD)	
	PT+PRP (n=25)	PT+PRP (n=25)
Values	103.60 (14.39)	93.20 (14.64)

Unpaired t test, p value=0.015, significant.

Comparison of range of motion (internal rotation) between study groups (n=50)

Internal rotation was significantly higher in group A as compared to group B.

Mean±SD of Abduction in group A was 44.00±10.80 which was significantly higher as compared to group B (31.60±8.98) (p value≤0.001) by unpaired t test (Table 3).

Table 3: Comparison of range of motion between study groups (n=50).

Internal rotation	Group, mean (SD)	
	PT+PRP (n=25)	PT+PRP (n=25)
Values	44.00 (10.80)	31.60 (8.98)

Unpaired t test, p value <0.001, significant.

DISCUSSION

The standard method for treating frozen shoulders focuses on alleviating pain and restoring joint movement to ensure proper function. Non operative treatment for AC includes physical therapy, pharmacological therapy in the form of non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroid intra-articular or sub acromial injections, sodium hyaluronate intra-articular injection, suprascapular nerve blocks. Operative treatment includes hydrodilation, manipulation under anesthesia, arthroscopic capsulotomy and open capsulotomy, however significant morbidity is associated with these operative procedures.

In our study, we evaluated the effectiveness of intra-articular PRP (IA-PRP) combined with physiotherapy (PT) versus PT alone in treating adhesive capsulitis (AC). The IA-PRP injections resulted in better pain relief and greater functional improvement after 24 weeks compared to PT alone. The physiotherapy group also demonstrated significant improvement in shoulder range of motion (ROM), particularly in both active and passive shoulder abduction, as well as internal and external rotations. At the end of 24 weeks, IA-PRP group showed significant improvement in VAS score as compared to PT alone. Patients in the IA-PRP group consumed less acetaminophen, indirectly confirming that they experienced better pain relief compared to the PT-only group. Additionally, treatment satisfaction was higher among patients who received the IA-PRP injection.

Adhesive capsulitis is proposed as an inflammatory and fibrotic condition. The efficacy of corticosteroid injections in treating adhesive capsulitis is attributed to their ability to reduce inflammation, thereby improving clinical outcomes.[16] Conversely, the precise mechanism of action of PRP remains unclear due to its dual proinflammatory and anti-inflammatory properties. Literature suggests that PRP not only releases a range of growth factors essential for tissue repair (such as platelet-derived growth factor, transforming growth factor-β, vascular endothelial growth factor, and epidermal growth factor), but also releases a significant amount of RANTES/CCL5 from its α-granules.[10,13,17] RANTES/CCL5 (regulated on activation, normal T expressed and secreted/C-C motif chemokine ligand 5) belongs to the C-C chemokine β subfamily, playing a role in regulating leukocyte recruitment to inflammation sites and modulating inflammatory and nociceptive responses.[18] Additionally, RANTES/CCL5 inhibits numerous cytokines released by basophils and reduces the concentration of lipoxin A4 (an anti-inflammatory marker), further diminishing the number of inflammatory cells.

In this study, the notable enhancements observed in patients from the IA-PRP group could be attributed to PRP potentially exerting significant influences across the various stages of tissue healing: inflammation, proliferation, and remodeling, particularly with respect to capsular healing. However, additional research is required to validate these findings and delve into the specific mechanisms through which PRP operates. It's crucial to determine whether the improvements are temporary or if PRP holds a more substantial role with disease-modifying capabilities.

Our method yielded a mean platelet count of 700×103/µl, representing a more than four-fold increase compared to the established standard in prior studies.[17,18] The presence of leukocytes in PRP is a contentious issue regarding their impact on platelet efficacy. While some studies caution against including leukocytes due to potential inflammatory reactions, others highlight their benefits like antibacterial and immunological resistance.[19,20] In our PRP product, the

mean leukocyte concentration was 0.3×103/µl (range: 0.1–1.5×103/µl), significantly lower than the recommended level by the American Association of Blood Banks.[21] We administered freshly prepared PRP within 30 minutes of preparation, following Blajchman's findings that prolonged platelet storage can alter properties and reduce functional capabilities, including α-granule degranulation.[14]

Three patients within the IA-PRP group experienced discomfort and mild pain near the puncture site. No significant complications, particularly inflammation or infection linked to IA injections, or severe adverse events were documented during the treatment and follow-up period.

Kothari et al found that patients in the IA-PRP group exhibited significant improvements in pain and shoulder motion compared to the IA-CS group.[22] However, their study was limited by the lack of a standardized PRP preparation technique. Similarly, studies by Scarpone et al and Tahririan et al demonstrated improvements in pain and function after a single PRP injection in patients with rotator cuff tendinopathy.[23,24] However, these studies were limited as they focused on patients with rotator cuff tendinopathy and administered injections extra-articularly, thus did not compare the effects of IA-PRP injections for frozen shoulder.

Several limitations warrant acknowledgment. The study's duration was confined to 24 weeks. We did not delve into the cost-benefit analysis of treatments. The compliance with the home rehabilitation program was not assessed. We did not employ any specialized technique to activate platelets in the PRP post-preparation. This activation principle has been utilized in numerous studies to attain the desired growth factor levels. We did not measure the growth factor levels in our PRP product, as several studies have indicated that growth factor dose-response curves are non-linear and may be inhibitory at higher concentrations.

CONCLUSION

In instances of AC, both sets of participants showed progress after 12 weeks. Yet, IA injections containing PRP offered notable pain reduction and enhanced functional recovery in shoulder mobility compared to solely undergoing PT. This research highlights PRP's growing importance in managing persistent musculoskeletal issues such as AC, especially when corticosteroids are unsuitable due to conditions like diabetes mellitus or patient refusal. Nonetheless, longer-term randomized multicenter trials are crucial to confirm these results and reevaluate symptom amelioration.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Zuckerman JD, Rokito A. Frozen shoulder: a consensus definition. J Shoulder Elbow Surg. 2011;20:322-5.
2. Tasto JP, Elias DW. Adhesive capsulitis. Sports Med Arthrosc Rev. 2007;15:216-21.
3. Robinson CM, Seah KT, Chee YH, Hindle P, Murray IR. Frozen shoulder. J Bone Joint Surg Br. 2012;94:1-9.
4. Mezian K, Coffey R, Chang KV. Frozen Shoulder. In: StatPearls. Treasure Island (FL): StatPearls Publishing. 2023.
5. Jayson MI. Frozen shoulder: adhesive capsulitis. Br Med J (Clin Res Ed). 1981;283:1005-6.
6. Walmsley S, Osmotherly PG, Rivett DA. Movement and pain patterns in early stage primary/idiopathic adhesive capsulitis: a factor analysis. Physiotherapy. 2014;100:336-43.
7. Wolf EM, Cox WK. The external rotation test in the diagnosis of adhesive capsulitis. Orthopedics. 2010;33.
8. Uppal HS, Evans JP, Smith C. Frozen shoulder: A systematic review of therapeutic options. World J Orthop. 2015;6:263-8.
9. Rangan A, Hanchard N, McDaid C. What is the most effective treatment for frozen shoulder? BMJ. 2016;354:i4162.
10. Chan HBY, Pua PY, How CH. Physical therapy in the management of frozen shoulder. Singapore Med J. 2017;58(12):685-9.
11. Marx RE. Platelet-rich plasma: evidence to support its use. J Oral Maxillofac Surg. 2004;62(4):489-96.
12. Gautam VK, Verma S, Batra S, Bhatnagar N, Arora S. Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: clinical and ultrasonographic evaluation. J Orthop Surg. 2015;23(1):1-5.
13. Barman A, Mukherjee S, Sahoo J, Maiti R, Rao PB, Sinha MK, et al. Single Intra-articular Platelet-Rich Plasma Versus Corticosteroid Injections in the Treatment of Adhesive Capsulitis of the Shoulder: A Cohort Study. Am J Phys Med Rehabil. 2019;98(7):549-57.
14. Blajchman MA. Novel platelet products, substitutes and alternatives. Transfus Clin Biol. 2001;8:267-71.
15. Tveitå EK, Ekeberg OM, Juel NG, Bautz-Holter E. Responsiveness of the shoulder pain and disability index in patients with adhesive capsulitis. BMC Musculoskelet Disord. 2008;9:161.
16. Koh KH. Corticosteroid injection for adhesive capsulitis in primary care: a systematic review of randomised clinical trials. Singapore Med J. 2016;57(12):646-57.
17. Kesikburun S, Tan AK, Yilmaz B, Yaşar E, Yazicioğlu K. Platelet-rich plasma injections in the treatment of chronic rotator cuff tendinopathy: a randomized controlled trial with 1-year follow-up. Am J Sports Med. 2013;41(11):2609-16.

18. Foster TE, Puskas BL, Mandelbaum BR, Gerhardt MB, Rodeo SA. Platelet-rich plasma: from basic science to clinical applications. Am J Sports Med. 2009;37(11):2259-72.
19. Moojen DJ, Everts PA, Schure RM, Overdevest EP, van Zundert A, Knape JT, et al. Antimicrobial activity of platelet-leukocyte gel against Staphylococcus aureus. J Orthop Res. 2008;26(3):404-10.
20. Mazzocca AD, McCarthy MB, Chowaniec DM, Cote MP, Romeo AA, Bradley JP, et al. Platelet-rich plasma differs according to preparation method and human variability. J Bone Joint Surg Am. 2012;94(4):308-16.
21. Sharma RR, Marwaha N. Leukoreduced blood components: Advantages and strategies for its implementation in developing countries. Asian J Transfus Sci. 2010;4(1):3-8.
22. Kothari SY, Srikumar V, Singh N. Comparative Efficacy of Platelet Rich Plasma Injection, Corticosteroid Injection and Ultrasonic Therapy in the Treatment of Periarthritis Shoulder. J Clin Diagn Res. 2017;11(5):RC15-8.
23. Scarpone M, Rabago D, Snell E, Demeo P, Ruppert K, Pritchard P, et al. Effectiveness of Platelet-rich Plasma Injection for Rotator Cuff Tendinopathy: A Prospective Open-label Study. Glob Adv Health Med. 2013;2(2):26-31.
24. Tahririan MA, Moezi M, Motififard M, Nemati M, Nemati A. Ultrasound guided platelet-rich plasma injection for the treatment of rotator cuff tendinopathy. Adv Biomed Res. 2016;5:200.

Cite this article as: Avhad TA, Lombar S, Kalra N. Comparison of clinical and functional outcomes of physical therapy alone versus additional intraarticular injection of platelet rich plasma in treatment of frozen shoulder in Indian population. Int J Res Orthop 2024;10:769-75.