

Secondary Logo

Journal Logo



Advanced Search

Welcome Ovid Subscriber!

Your institution's Ovid subscription entitles you to view the full text of articles on the American Journal of Physical Medicine & Rehabilitation journal website.

Single Intra-articular Platelet-Rich Plasma Versus Corticosteroid Injections in the Treatment of Adhesive Capsulitis of the Shoulder

A Cohort Study

Barman, Apurba MD; Mukherjee, Somnath MD; Sahoo, Jagannatha DNB; Maiti, Rituparna MD; Rao, Parnandi Bhaskar MD; Sinha, Mithilesh Kumar MS; Sahoo, Dibyajyoti MD; Tripathy, Sujit Kumar MS; Patro, Binod Kumar MD; Bag, Nerbadyswari Deep MD

American Journal of Physical Medicine & Rehabilitation: July 2019 - Volume 98 - Issue 7 - p 549–557

doi: 10.1097/PHM.0000000000001144

Original Research Articles

Abstract **Author Information** **Authors** **Article Outline** **Outline** **Article Metrics** **Metrics**

Objective 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 18–70 yrs of either sex, diagnosed with adhesive capsulitis of shoulder, with less than 6-mo duration, were included. In intra-articular corticosteroid (IA-CS, control) group, 30 patients received a single injection (4 ml) of IA-CS and in IA-PRP (test) group, 30 patients received single IA-PRP injection (4 ml) into the glenohumeral joint under ultrasound guidance. All patients were prospectively followed for 12 wks.

Results Twenty-eight patients in IA-PRP group and 27 in IA-CS group finished the entire 12-wk study period. At 12 wks, decrements in visual analog scale and total shoulder pain and disability index scores, in IA-PRP group, were 58.4 and 55.1, compared with 48.7 and 45.8 in IA-CS group. In range of movement, IA-PRP group showed significant improvement in passive abduction (-50.4 vs. -39.4), internal (-36.8 vs. -25.8), and external rotations (-35.4 vs. -25.9) compared with IA-CS group, respectively. No major complications were observed in any patients.

Conclusions At 12-wk 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, and shoulder range of movement in patients with adhesive capsulitis of the shoulder.

From the Departments of Physical Medicine and Rehabilitation (AB, JS), Transfusion Medicine (SM, DS), Pharmacology (RM), Anesthesia and Intensive Care (PBR), General Surgery (MKS), Orthopaedics (SKT), Community and Family Medicine (BKP), and Radiodiagnosis (NDB), All India Institute of Medical Sciences, Bhubaneswar, India.

All correspondence should be addressed to: Apurba Barman, MD, Department of PM&R, All India Institute of Medical Sciences, Bhubaneswar, Patrapada, Dumuduma, Bhubaneswar, Odisha, India 751019.

The study was supported by Institutional Intramural Research Grant, All India Institute of Medical Sciences, Bhubaneswar, India (Grant Number IMF 21/2016).

Financial disclosure statements have been obtained, and no conflicts of interest have been reported by the authors or by any individuals in control of the content of this article.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.ajpmr.com).

Online date: January 23, 2019

- Abstract
- METHODS
 - Participants
 - Study Design
 - Intervention
 - Outcome Measures
 - Statistical Analysis
- RESULTS
 - Clinical Characteristics of the Patients
 - Changes of the VAS
 - Changes in the ROM of the Shoulder Joint
 - Changes of Shoulder Function
 - Satisfaction Scale
 - Acetaminophen Usage
- DISCUSSION
- CONCLUSIONS
- REFERENCES

- Supplemental Digital Content

Adhesive capsulitis (AC) is one of the common causes of shoulder pain and disability in the upper extremity. It affects the functions of glenohumeral (GH) joint, limiting both active and passive movements of the shoulder.¹ Limitation of passive range of movements (ROMs) of the shoulder, particularly external rotation, has remained pivotal to the clinical diagnosis of AC. The incidence of AC is 2%–5% in the general population, whereas prevalence among diabetic patients is up to 20%.¹

The goals of treatment of AC are to relieve pain, restore movement, and ultimately regain shoulder function.¹ Intra-articular corticosteroid (IA-CS) injection still remains one of the most common procedures for treating AC because of its cost-effectiveness and acceptance among patients.^{1,2} Studies have shown that CS into the shoulder joint provides symptomatic relief and limits the development of capsular fibrosis.^{1,2} However, CS injection has been found, associated with hyperglycemia, detrimental effects on articular cartilage, increased risk of tendon rupture, local skin depigmentation, and atrophy of subcutaneous tissue.³ The American Diabetes Association, American College of Sports Medicine, American Academy of Orthopaedic Surgeons, and American Medical Society for Sports Medicine have made no recommendations regarding CS injections in patients with diabetes mellitus (DM).³ Considering the possible side effects of CS injections, it is important for both physicians and patients to know to develop the most appropriate treatment plan for patients with AC, who are contraindicated to CS injection or who are not willing for CS injection.

Recently, new evidence has emerged on the effectiveness of platelet-rich plasma (PRP) injection in the treatment of chronic tendon and muscle injuries, tendinopathies, osteoarthritis etc.^{4–11} In PRP therapy, autologous “platelets,” obtained by whole-blood centrifugation, are concentrated and then reinjected into the affected joint. Studies have suggested that injection with PRP is safe and it has antinociceptive, anti-inflammatory, and regenerative properties. Platelet-rich plasma could stimulate the healing process of tissues with chronic injuries and relieve pain and stiffness of the joints.^{5–8,10,11} However, its evidence of effectiveness in patients with AC is limited.

The objective of this study was to compare the effects of a single IA-PRP injection with a conventional single IA-CS injection, in conjunction with a supervised exercise program, on pain and shoulder functions in patients with AC. The human body has a remarkable ability to heal itself; hence, we hypothesize that reinjecting concentrated platelets will reduce the inflammation of the synovium and facilitate the natural healing process of the joint capsule, which ultimately will provide a better improvement in pain and stiffness of the shoulder joint, compared with IA-CS injection, in patients with AC.

METHODS

Participants

Participants were outpatients at a rehabilitation clinic of a tertiary care teaching hospital, India, who were diagnosed as having primary AC between February 2017 and February 2018. All patients underwent a standardized history, physical examination, radiological, and ultrasonography evaluation. Active and passive ROMs, painful arc/impingement test, resisted test, and strength of muscles were assessed in both arms.

Inclusion criteria were patients with AC with duration of symptoms less than 6 mos, who had a normative radiograph finding of the affected shoulder, and moderate to severe pain (visual analog scale [VAS] score ≥ 50) and limitation of both active and passive movements of the GH joint of 25% or more in 2 or more directions (abduction, flexion, external rotation, internal rotation), as compared with the contralateral shoulder, and were aged 18–70 yrs. If bilateral shoulders were involved and qualify for inclusion, only the dominant arm was considered for intervention. Patients with secondary AC (secondary to inflammatory joint disease, structural/functional limitations in the shoulder joint from any other preexisting musculoskeletal pathology or neurologic disorder), with anemia (hemoglobin level <9 g/dl), uncontrolled DM, poor cognitive status, who were unable to follow exercise program, and patients who had previously undergone any IA injection/invasive procedure/surgery in the shoulder joints were excluded from the study.

The study was approved by the institutional review board and all patients provided written informed consent. This study conformed to all STROBE guidelines and reports the required information accordingly (see Supplemental Checklist, Supplemental Digital Content 1, <http://links.lww.com.ezproxy.library.ubc.ca/PHM/A739>).

Study Design

This is a prospective cohort study. A schematic diagram of the study is shown in Figure 1. After obtaining informed consent, 60 patients with AC were recruited in the present study. In control group (IA-CS group), 30 patients received a single injection (4 ml) of CS injection, and in the test group (IA-PRP group), 30 patients received a single IA-PRP injection (4 ml) into the GH joint. Patients with DM or with a history of CS side effects received PRP and other patients received CS injection. Two milliliter (40 mg) of methyl prednisolone acetate was mixed with 2 ml 2% lignocaine (total 4 ml) to prepare 4 ml of CS injection. The patients in the test group were matched with the control group depending on the duration of the disease.

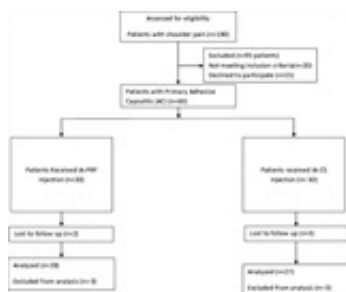


FIGURE 1

The PRP was prepared by the single centrifugation technique^{4,12,13} using bench top centrifuge System (Eppendorf AG Centrifuge 5702), in accordance with standard operating procedure. Twenty-four milliliter of venous blood was drawn from the patient's uninvolved arm with an 18-gauge needled syringe, with a single puncture, atraumatically to minimize tissue damage and platelet activation, during blood sampling. The blood sample was then equally divided into two specially designed disposable bio-kit tubes (Plasmamed PRP Kit) of 12 ml capacity each, containing anticoagulant citrate dextrose-A of 1.5 ml to prevent the coagulation cascade. A peripheral complete blood count was also obtained at the time of initial blood draw, by the automated cell counter (Sysmex XP-100) from the left out blood sample. The two PRP kit tubes were made up and down three times to mix the blood with the anticoagulant. The tubes were then centrifuged for 14 mins at 1800 rpm, and approximately 5 ml (2.5 ml in each tube) of PRP was

obtained from the two tubes. Of this, 4 ml of PRP, without adding any buffering or activating agent, was aspirated aseptically from the two tubes by the spinal needle in a class IIA biosafety cabinet (Waiometra; Associated Scientific Technologies) for injecting the patient. The rest of 1-ml PRP was sent for analysis of platelet count by automated cell counter. Total platelet count was measured from the final PRP product, and it was also compared with the initial platelet count taken from the whole-blood sample. All procedures were performed under sterile conditions. Within 30 mins of preparation, PRP injection was given to the patients. The whole procedure of preparation of PRP was done in the Laboratory of Department of Transfusion Medicine and Blood Bank under the guidance of Transfusion Medicine Physician.

Intervention

All the injections were performed by an experienced physiatrist (lead author) with ultrasound equipment SonoSite M-Turbo, using a 13- to 6-MHz linear array transducer. For IA injection into GH joint, the posterior approach was followed for both intervention groups.^{14,15} The patients were seated on a chair, in an upright position with their hands positioned on their thighs. A 23-gauge, 7-cm-long needle was inserted parallel to the ultrasound probe in a semioblique plane until the tip of the needle entered the GH joint (Fig. 2). The expansion of the articular capsule was checked while the fluid (PRP or CS) was being injected. All injections, IA-PRP and IA-CS, were given in proper aseptic condition, in operation theater. The patients were instructed to rest from overhead activity and rotary movements of the shoulder during the first 2 days. Once the procedure was over, patients were handed over picture leaflets and proper instructions were given about the home exercise program for increasing ROM, including Codman, pendulum exercises, posterior and inferior shoulder stretching exercises, scapular stabilization exercises, and a wall-climbing exercise. The exercises were to be started 2 days after injection and to be performed two times a day lasting 20 mins each time.



FIGURE 2

During the observational period of 12 wks, nonsteroidal anti-inflammatory drugs were not allowed. However, patients were allowed to take oral acetaminophen (1 g) tablets for severe pain or discomfort, if required, up to maximum 3 g/d. All patients were asked to stop medications 48 hrs before follow-up assessment. The patients were strictly advised to maintain records of receiving tablets and an exercise notebook to track their exercise frequency, duration, and any difficulties. The notebooks were checked at each follow-up visit. Calls were also made to patients to encourage continuous exercises and remind them not to receive any additional medication and or physical agents.

Outcome Measures

Baseline characteristics were collected from all patients. Outcome measures were assessed at baseline and at 3, 6, and 12 wks after the injection. Patients were requested to report any adverse effects at each visit. A blinded assessor (one physiatrist, not involved in the intervention) examined the patient and recorded the primary and secondary outcomes at the time of enrolment of the study and during follow-up visits (3, 6, and 12 wks after the injection).

The intensity of shoulder pain was measured using VAS.⁵ The patient answered the question “With respect to the worst pain you have experienced in your life, what was the average level of your shoulder pain in the past one week?” A 100-mm VAS score (0, no pain; 100, worst pain possible) was used as primary outcome measure. Secondary outcome measures were the Shoulder Pain And Disability Index (SPADI),¹⁶ active and passive ROM of the shoulder using goniometry (flexion, extension, abduction, internal, and external rotation), and satisfaction. Shoulder Pain and Disability Index is a self-reported measure developed to evaluate shoulder pathology.¹⁶ Patients by themselves or with the help of relatives filled up the SPADI questionnaires. It consists of 13 questions that are divided into two domains: pain (5 items) and disability (8 items). Each domain score is equally weighed and added to get a total percentage score between 0 (best) and 100 (worst).¹⁵

The standard technique of measuring ROM of the shoulder joint was followed, and universal goniometer with two arms, was used to measure the ROM. The active and passive shoulder flexion, extension, and abduction were measured, whereas the patient was in a sitting position, and the internal rotation and external rotation were checked while the patient was in the supine position. Internal and external rotations were measured in 90-degree abduction of the shoulder and 90-degree flexion of the elbow position. If abduction of shoulder measured less than 90 degrees, maximum possible abduction was achieved before measuring the internal and external rotations. The patient was positioned to the same degree of abduction, to measure the internal and external rotations during follow-up visits. Patient satisfaction was assessed at 12 wks using a three-item scale (satisfied, partly satisfied, not satisfied).⁴

Statistical Analysis

A power analysis program was used to calculate the number of patients required. Sample size calculation was done considering VAS as a primary outcome measure. This study was designed to have 80% power to detect a difference of 10-point improvement in VAS scoring between both groups (pooled standard deviation = 14, two-sided *t* test $\alpha = 0.05$). To achieve this, 30 participants per group were needed. Statistical analyses were performed using the SPSS program (Statistical Package of Social Sciences, Chicago, IL) Version 22.0. Data on continuous variables are presented as the mean \pm SD and categorical data in percentage or proportion. The differences in the changes of all parameters at different time points were compared by repeated-measure analysis of variance. A post hoc Bonferroni test was used to compare the change in different parameter from baseline to second, third, and fourth visit. A *P* value of <0.05 was considered to be statistically significant in all tests.

RESULTS

Clinical Characteristics of the Patients

Sixty subjects were recruited in this study. Twenty-eight of 30 patients in the IA-PRP group and 27 of 30 patients in the IA-CS group finished the entire 12-wk study period. Five subjects did not return for all follow-up, two in IA-PRP group and three in IA-CS group. Table 1 lists the demographic and clinical characteristics of the study subjects. No

disparity was found between the baselines characteristics of both groups including age, body mass index, duration of symptoms, initial pain score, active and passive movements of shoulder, and SPADI scores (Table 1). The dominant side was affected in most cases in both groups.

Parameters	IA-PRP Group (n = 29)	IA-CS Group (n = 27)	P ^a
Sex, male/female	3/4	10/17	0.76
Age, yr	50.0 ± 6.31	50.26 ± 5.94	0.88
Body mass index, kg/m ²	24.77 ± 2.87	25.21 ± 2.96	0.49
Duration of disease, mean ± SD, mo	4.02 ± 1.04	4.11 ± 0.9	0.26
Involved side			
Dominant/non-dominant	4/3	5/4	0.99
Pain with activity, mean ± SD	76.3 ± 9.9	71.5 ± 8.7	0.24
Range of Motion, degree			
Flexion			
Active	78.0 ± 12.1	78.9 ± 13.3	0.10
Passive	95.0 ± 14.4	100.0 ± 10.4	0.09
Extension			
Active	22.1 ± 6.1	19.9 ± 3.9	0.14
Passive	28.6 ± 4.6	29.1 ± 4.7	0.89
Abduction			
Active	47.0 ± 8.1	42.6 ± 11.6	0.07
Passive	87.0 ± 11.3	89.0 ± 11.2	0.71
Internal rotation			
Active	15.9 ± 6.3	16.1 ± 4.6	0.90
Passive	25.6 ± 3.9	26.9 ± 4.3	0.30
External rotation			
Active	19.0 ± 3.7	19.9 ± 3.1	0.29
Passive	25.0 ± 6.4	27.6 ± 5.4	0.10
SPADI (total)	49.4 ± 12.3	46.5 ± 9.6	0.10

^aValues are expressed as n or mean ± SD.
^bUnpaired t-test/Fisher's exact test for two group comparison (P < 0.05).

TABLE 1

Changes of the VAS

After receiving IA-PRP injections, pain on activity, assessed by the VAS scales, the primary outcome of the study, reduced significantly in comparison with IA-CS group (Tables 2, 3). Although initially no significant difference in the amount of pain reduction was observed at 3-wk follow-up visits (P = 0.06), later at the end of 6 and 12 wks, significant differences were observed among both groups (Table 4, Fig. 3). Figure 3 shows the changes in VAS pain scores over time.

Time	VAS		P ^a	VAS		P ^a
	IA-PRP	IA-CS		IA-PRP	IA-CS	
Baseline	76.3 ± 9.9	71.5 ± 8.7	0.24	76.3 ± 9.9	71.5 ± 8.7	0.24
3 weeks	68.5 ± 10.2	65.8 ± 9.5	0.06	68.5 ± 10.2	65.8 ± 9.5	0.06
6 weeks	58.2 ± 11.5	62.1 ± 10.8	0.02	58.2 ± 11.5	62.1 ± 10.8	0.02
12 weeks	52.1 ± 12.8	58.9 ± 11.4	0.01	52.1 ± 12.8	58.9 ± 11.4	0.01

^aUnpaired t-test for two group comparison (P < 0.05).

TABLE 2

Time	VAS		P ^a	VAS		P ^a
	IA-PRP	IA-CS		IA-PRP	IA-CS	
Baseline	76.3 ± 9.9	71.5 ± 8.7	0.24	76.3 ± 9.9	71.5 ± 8.7	0.24
3 weeks	68.5 ± 10.2	65.8 ± 9.5	0.06	68.5 ± 10.2	65.8 ± 9.5	0.06
6 weeks	58.2 ± 11.5	62.1 ± 10.8	0.02	58.2 ± 11.5	62.1 ± 10.8	0.02
12 weeks	52.1 ± 12.8	58.9 ± 11.4	0.01	52.1 ± 12.8	58.9 ± 11.4	0.01

^aUnpaired t-test for two group comparison (P < 0.05).

TABLE 3

Time	VAS		P ^a	VAS		P ^a
	IA-PRP	IA-CS		IA-PRP	IA-CS	
Baseline	76.3 ± 9.9	71.5 ± 8.7	0.24	76.3 ± 9.9	71.5 ± 8.7	0.24
3 weeks	68.5 ± 10.2	65.8 ± 9.5	0.06	68.5 ± 10.2	65.8 ± 9.5	0.06
6 weeks	58.2 ± 11.5	62.1 ± 10.8	0.02	58.2 ± 11.5	62.1 ± 10.8	0.02
12 weeks	52.1 ± 12.8	58.9 ± 11.4	0.01	52.1 ± 12.8	58.9 ± 11.4	0.01

^aUnpaired t-test for two group comparison (P < 0.05).

TABLE 4

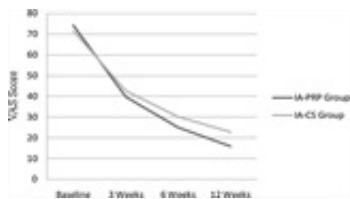


FIGURE 3

Changes in the ROM of the Shoulder Joint

Both groups showed improvements in active and passive shoulder ROMs at the end of 12 wks (Tables 2, 3). In intergroup comparison, statistically significant improvements were noticed in both active and passive shoulder abduction, internal, and external rotations in IA-PRP group.

Changes of Shoulder Function

The SPADI scores decreased significantly in both IA-PRP and IA-CS groups (Tables 2, 3). However, in intergroup comparisons, the improvement was more significant statistically in the IA-PRP group at 12 wks (Table 4). Figure 4 shows the changes in the SPADI scores over time.

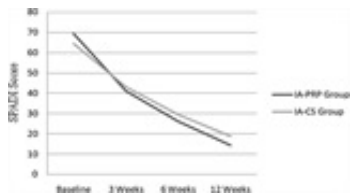


FIGURE 4

Satisfaction Scale

At the end of 12 wks, 75% ($n = 21$) of patients were satisfied, 18% ($n = 5$) were partly satisfied, and 7% ($n = 2$) were not satisfied in IA-PRP group. In IA-CS group, 52% ($n = 14$) were satisfied, 33% ($n = 9$) were partly satisfied, and 15% ($n = 4$) were not satisfied with the intervention.

Acetaminophen Usage

During 12-wk follow-up period, 39% ($n = 11$) of patients in IA-PRP group did not receive any acetaminophen tablets, 43% ($n = 12$) patients received 1- to 2-g acetaminophen tablets, 18% ($n = 5$) of patients received 3- to 4-g tablets. Whereas in IA-CS group, 19% ($n = 5$) of patients did not receive any acetaminophen tablets, 11% ($n = 3$) patients received 1- to 2-g acetaminophen tablets, 37% ($n = 10$) of patients received 3- to 4-g tablets, and 33% ($n = 9$) of patients received more than 4-g tablets.

DISCUSSION

In the present study, we compared the effectiveness of IAPRP and IA-CS injections in the treatment of AC. Intra-articular platelet-rich plasma injection provided better pain relief and greater functional improvement compared with IA-CS injection at 12 wks. Intra-articular platelet-rich plasma group also showed significant improvement in shoulder ROM, especially in both active and passive shoulder abduction, internal, and external rotations. Immediately after interventions in the first 3 wks, both groups showed a significant decrease in pain scores. More than 50% pain improvements, as measured by VAS pain scores, were observed in both groups at 3 wks. At 3 wks, no statistically significant differences were obtained among the two groups, but later at the end of 12 wks, IA-PRP group showed significant improvement in pain score. Patients recruited in IA-PRP group consumed less amount of acetaminophen, which further indirectly confirmed that patients in IA-PRP group achieved better pain relief compared with IA-CS groups. Treatment satisfaction was higher among patients, who received IA-PRP injection. A similar trend was also observed by Kothari et al.⁵ in their study, IA-PRP group patients showed significant improvements in terms of pain and shoulder motion compared with IA-CS group, but this study was complicated by lack of standardized PRP preparation technique. Scarpone et al.¹⁷ and Tahririan et al.¹⁸ in their studies also showed improvements in pain and function after a single injection of PRP in patients with rotator cuff tendinopathy. A case study, reported by Aslani et al.⁹ in 2016, also showed good results with PRP in frozen shoulder. However, Kesikburun et al.¹² failed to show significant improvements with PRP injection, compared with placebo injection in patients with rotator cuff tendinopathy. However, most of these studies were done on patients with rotator cuff tendinopathy and injections were given extra-articularly, in the subacromial bursa, and they did not compare effects of IA-PRP injection with IA-CS injection.

The strengths of the present study included a precise definition of the conditions, recruitment of all population with AC, ultrasound-guided injections, and analysis of pain and functional outcomes at different time points, which provided high-quality evidence for the effectiveness of PRP and CS injections and its influence over time. Demographic variables and baseline characteristics, among patients recruited across the groups, were comparable; no statistically significant differences were obtained across the study populations. In this study, ultrasound-guided IA injections were administered to all patients. One single operator, experienced in ultrasound-guided IA injections, administered all injections. The accuracy of the US-guided injection was determined by capsular distension during the injection in real time.

Adhesive capsulitis is postulated as an inflammatory and fibrotic disease.¹ Corticosteroid injections have shown that treatment effect for AC through its reduction of the inflammation has led to the improvement of clinical outcomes.¹ On the contrary, detailed mechanism of action of PRP is not well understood, because it has both proinflammatory and anti-inflammatory properties. It is evident from the literature that PRP not only releases pool of growth factors (eg, platelet-derived growth factor, transforming growth factor- β , vascular and epidermal endothelial growth factor),^{9,12,19} which are essential for tissue repair, but also releases a considerable amount of RANTES/CCL5 (a major monocyte chemo attractant) from its α -granules.²⁰ RANTES/CCL5 (regulated on activation, normal T expressed and secreted/C-C motif chemokine ligand 5) is a member of the C-C chemokine β subfamily that regulates the recruitment of leukocytes at sites of inflammation and attenuates inflammatory and nociceptive responses.²⁰ RANTES/CCL5 also inhibits many cytokines released by basophil and decrease the concentration of lipoxin A4 (anti-inflammatory marker), which further depress the number of inflammatory cells.²⁰ Apart from that, PRP releases hepatocyte growth factor and tumor necrosis factor α , which are having potent anti-inflammatory effect.²¹ The antinociceptive effect of PRP may be due to the augmentation of cannabinoid receptors, CB1 and CB2.²² In this study, greater improvements in patients, recruited in IA-PRP group, could be explained by the fact that PRP might

have profound effects on all phases of tissue healing: inflammatory, proliferative, and remodeling phases of capsular healing in AC. Most probably, IA-PRP modulated the cytokine levels of synovial fluid and reduced synovial membrane hyperplasia in a more effective way compared with IA-CS, which ultimately translated into increased pain reduction in the affected shoulder. Because pain reduced significantly and overall joint homeostasis improved rapidly in the IA-PRP group, patients might have performed home exercises more accurately, thus leading to an improvement in the overall clinical outcome, even if temporarily. These mechanistic rationales are based on the scientifically informed suspicions, but not based on data from this study, because this study did not evaluate the molecular basis of action of PRP on capsular healing. However, further studies are needed to confirm the results obtained and to understand the detailed mechanisms by which PRP works and to evaluate whether there is only a temporary improvement or whether PRP plays a more important role through the disease-modifying properties.

Platelet concentration in PRP mainly determines the quality of the PRP¹² because the higher number of platelet in the PRP can commensurably produce a higher degree of clinical response.¹³ The mean platelet count achieved by our method was $696 \times 10^3/\mu\text{l}$. We obtained more than four-fold increase the number of platelets in PRP, which was regarded as standard and effective count as per previous studies.^{12,23} Presence of leucocytes in the PRP with their effects on the clinical efficacy of platelets is highly controversial. Few studies have recommended against the inclusion of leucocytes in PRP because they incite an inflammatory reaction, whereas others have reported the beneficial effect of leucocytes including antibacterial and immunological resistance.^{24,25} As described earlier, in this study, PRP was prepared by single centrifugation technique. Therefore, the mean concentration of leucocytes in our PRP product was $0.3 \times 10^3/\mu\text{l}$ (range: $0.1\text{--}1.5 \times 10^3/\mu\text{l}$), which was much less than standardized leucocyte reduced blood product as per American Association of Blood Bank guideline.²⁶ During PRP preparation, we did not use any commercial filter. The entire PRP preparation technique was standardized and validated by our transfusion medicine department. In this study, we injected freshly prepared PRP, within 30 mins of preparation, as Blajchman²⁷ reported that prolonged storage of platelets may change the shape and reduce the functional properties, including degranulation of α -granules.

Three patients in IA-PRP group and two in IA-CS group developed discomfort and mild pain near the puncture site. No major complications, especially inflammation or infection related to IA injections or severe adverse events, during the treatment and follow-up period in any group, were recorded over time.

Several limitations need to be acknowledged. Study duration was limited to 12 wks. We did not explore the cost-benefit analysis of treatments. Compliance with the home rehabilitation program was not measured. We did not use any special technique advocating the activation of platelets in the PRP after preparation. This activation concept has been used in many studies to achieve the desired growth factor level. We did not estimate the growth factor levels in our PRP product, because many studies^{28,29} have shown that the dose-response curves of growth factors are not linear and may be inhibitory at higher concentrations. We administered a single injection when few studies had shown that multiple injections at interval can provide better improvement than a single injection. We believed that subsequent rehabilitation exercises after single injection would be influential for long-term functional improvement.

CONCLUSIONS

In AC, both groups showed improvements at 12 wks. However, IA injection with PRP resulted in significant pain relief and greater functional improvement in shoulder motion, compared with IA-CS injection. This study highlights the growing importance of PRP in chronic musculoskeletal conditions such as AC, especially in clinical scenarios

where CS is contraindicated or refused by the patient. However, randomized multicenter trials with a long duration are needed to confirm the results obtained and to reassess the symptoms improvement.

REFERENCES

1. Koh KH: Corticosteroid injection for adhesive capsulitis in primary care: a systematic review of randomised clinical trials. *Singapore Med J* 2016;57:646–57
2. Chang KV, Wu WT, Han DS, et al: Static and dynamic shoulder imaging to predict initial effectiveness and recurrence after ultrasound-guided subacromial corticosteroid injections. *Arch Phys Med Rehabil* 2017;98:1984–94
3. Waterbrook AL, Balcik BJ, Goshinska AJ: Blood glucose levels after local musculoskeletal steroid injections in patients with diabetes mellitus: a clinical review. *Sports Health* 2017;9:372–4
4. Patel S, Dhillon MS, Aggarwal S, et al: Treatment with platelet-rich plasma is more effective than placebo for knee osteoarthritis: a prospective, double-blind, randomized trial. *Am J Sports Med* 2013;41:356–64
5. Kothari SY, Srikumar V, Singh N: Comparative efficacy of platelet rich plasma injection, corticosteroid injection and ultrasonic therapy in the treatment of periartthritis shoulder. *J Clin Diagn Res* 2017;1:RC15–8
6. Dai W-L, Zhou A-G, Zhang H, Zhang J: Efficacy of platelet-rich plasma in the treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. *Art Ther* 2017;33:659–70.e1
7. Jang SJ, Kim JD, Cha SS: Platelet-rich plasma (PRP) injections as an effective treatment for early osteoarthritis. *Eur J Orthop Surg Traumatol* 2013;23:573–80
8. Mishra A, Pavelko T: Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med* 2006;34:1774–8
9. Aslani H, Nourbakhsh ST, Zafarani Z, et al: Platelet-rich plasma for frozen shoulder: a case report. *Arch Bone Jt Surg* 2016;4:90–3
10. Filardo G, Kon E, Di Matteo B, et al: Platelet-rich plasma injections for the treatment of refractory Achilles tendinopathy: results at 4 years. *Blood Transfus* 2014;12:533–40
11. Descalzi F, Ulivi V, Cancedda R, et al: Platelet-rich plasma exerts antinociceptive activity by a peripheral endocannabinoid-related mechanism. *Tissue Eng Part A* 2013;19:2120–9
12. Kesikburun S, Tan AK, Yilmaz B, et al: 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;41:2609–16
13. Arora S, Agnihotri N: Platelet derived biomaterials for therapeutic use: review of technical aspects. *Indian J Hematol Blood Transfus* 2017;33:159–67
14. Chen CP, Lew HL, Hsu CC: Ultrasound-guided glenohumeral joint injection using the posterior approach. *Am J Phys Med Rehabil* 2015;94:e117–8
15. Lee DH, Yoon SH, Lee MY, et al: Capsule-preserving hydrodilatation with corticosteroid versus corticosteroid injection alone in refractory adhesive capsulitis of shoulder: a randomized controlled trial. *Arch Phys Med Rehabil* 2017;98:815–21
16. Uddin MM, Khan AA, Haig AJ, et al: Presentation of frozen shoulder among diabetic and non-diabetic patients. *J Clin Orthop Trauma* 2014;5:193–8
17. Scarpone M, Rabago D, Snell E, et al: Effectiveness of platelet-rich plasma injection for rotator cuff tendinopathy: a prospective open-label study. *Glob Adv Health Med* 2013;2:26–31
18. Tahririan MA, Moezi M, Motifard M, et al: Ultrasound guided platelet-rich plasma injection for the treatment of rotator cuff tendinopathy. *Adv Biomed Res* 2016;5:200

19. Gautam VK, Verma S, Batra S, et al: Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: clinical and ultrasonographic evaluation. *J Orthop Surg (Hong Kong)* 2015;23:1–5
20. Abdul Ameer LA, Raheem ZJ, Abdulrazaq SS, et al: The anti-inflammatory effect of the platelet-rich plasma in the periodontal pocket. *Eur J Dent* 2018;12:528–31
21. Bendinelli P, Matteucci E, Dogliotti G, et al: Molecular basis of anti-inflammatory action of platelet-rich plasma on human chondrocytes: mechanisms of NF- κ B inhibition via HGF. *J Cell Physiol* 2010;225:757–66
22. Lee HR, Park KM, Joung YK, et al: Platelet-rich plasma loaded hydrogel scaffold enhances chondrogenic differentiation and maturation with up-regulation of CB1 and CB2. *J Control Release* 2012;159:332–7
23. Foster TE, Puskas BL, Mandelbaum BR, et al: Platelet-rich plasma: from basic science to clinical applications. *Am J Sports Med* 2009;37:2259–72
24. Moojen DJ, Everts PA, Schure R-M, et al: Antimicrobial activity of platelet-leukocyte gel against *Staphylococcus aureus*. *J Orthop Res* 2008;26:404–10
25. Mazzocca AD, McCarthy MB, Chowaniec DM, et al: Platelet-rich plasma differs according to preparation method and human variability. *J Bone Joint Surg Am* 2012;94:308–16
26. Sharma RR, Marwaha N: Leukoreduced blood components: advantages and strategies for its implementation in developing countries. *Asian J Transfus Sci* 2010;4:3–8
27. Blajchman MA: Novel platelet products, substitutes and alternatives. *Transfus Clin Biol* 2001;8:267–71
28. Mooren RE, Hendriks EJ, van den Beucken JJ, et al: The effect of platelet-rich plasma in vitro on primary cells: rat osteoblast-like cells and human endothelial cells. *Tissue Eng Part A* 2010;16:3159–72
29. Ranly DM, McMillan J, Keller T, et al: Platelet-derived growth factor inhibits demineralized bone matrix-induced intramuscular cartilage and bone formation. A study of immunocompromised mice. *J Bone Joint Surg Am* 2005;87:2052–64

Keywords:

Adhesive Capsulitis; Platelet-Rich Plasma; Corticosteroid; Intra-articular

Supplemental Digital Content

- PHM_00_00_2019_01_21_BARMAN_AJPMR-D-18-00560_SDC1.pdf; [PDF] (496 KB)

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

^ Back to top



Never Miss an Issue

Get new journal Tables of Contents sent right to your email inbox

Get New Issue Alerts

Browse Journal Content

- Most Popular
- Current Issue
- Past Issues
- For Authors
- About the Journal
- Register on the website
- Subscribe
- Get eTOC Alerts

For Journal Authors

- Submit an article
- How to publish with us

Customer Service

- Activate your journal subscription [Activate Journal Subscription](#)
- Help [Browse the help center](#)
- Contact us at:

EMAIL:

TEL: (USA):

TEL: (Int'l):

customerservice@lww.com

800-638-3030 (within USA)

301-223-2300 (international)

- 
- 

[Privacy Policy \(Updated May 9, 2018\)](#) - [Legal Disclaimer](#) - [Terms of Use](#) - [Open Access Policy](#) - [Feedback](#) - [Sitemap](#) - [RSS Feeds](#) - [LWW Journals](#)

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

This website uses cookies. By continuing to use this website you are giving consent to cookies being used. For information on cookies and how you can disable them visit our [Privacy and Cookie Policy](#).

Got it, thanks!