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Original Article

Analysis of Results of Platelet-rich Plasma with Arthroscopic Acromioplasty and Arthroscopic Acromioplasty: A Comparative Study

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Abstract

Introduction: Platelet-rich plasma (PRP) is widely used to treat a variety of clinical conditions. It has been hypothesized that PRP augments tendon healing. The mechanism of action of PRP is not fully elucidated. Our study is to compare the coapplication of PRP and arthroscopic acromioplasty (AA) with AA regarding clinical and tissue effect.

Methods: The study was conducted on 85 patients diagnosed as rotator cuff tendinopathy (RCT). The patients were randomized into AA (40 patients) and AA + PRP injection (45 patients). Patients were followed for a minimum 1 year. The results were evaluated with visual analog scale and Oxford shoulder score and Bonar score.

Results: There was significant improvement occurs in both groups from baseline symptom. We have found no statistical difference between the groups. When Bonar scoring for tendinopathy was compared, there was a statistically significant difference was found. The improved tendon healing was found in AA + PRP group.

Conclusion: AA significantly improves symptoms of RCT. In combination with PRP significantly improve tendon healing on histopathology. However, further studies with a larger and more varied ethnic and occupations group may be warranted to bring certainty in this dilemma.

Key words: Arthroscopic acromioplasty, Platelet-rich plasma, Rotator cuff tendinopathy

INTRODUCTION

Rotator cuff tendinopathy (RCT) is an important condition of the upper extremity, affecting 1 in 50 adults.[1] It is the third most common musculoskeletal problem over age of 65 years.[2-4] It causes shoulder pain and loss of function. Its greatest impact is on workers with repetitive and high-load upper extremity tasks and on athletes leading to significant morbidity, affecting activities of daily living, recreation, and work life.[5,6]

The exact pathophysiology of pain in rotator cuff disease is not known.[3] The patho-etiology of RCT can be attributed to extrinsic and intrinsic mechanisms, as well as to environmental factors. Shoulder impingement is the main extrinsic cause of RCT. It causes mechanical compression of the external portion (bursal side) of the tendon. Upon repeated compression during movement, the coracoacromial ligament also thicken, decreasing the subacromial space. The anatomical variants (acromial shape, subacromial joint spurs, and acromioclavicular joint spurs) can lead to RCT. Furthermore, the angle and shape of the acromion could be a possible cause of the pathology. Overuse activity coupled with coracoacromial arch changes leads to decreasing the subacromial space which has a significant effect on tendon injury.

Intrinsic mechanisms are associated with the tendon itself and can be from aging, altered biology, microvascular blood supply, degeneration, tendon overload, overuse, or trauma. Histopathology studies reveal mainly degenerative changes with a fibroblastic and a vascular response known as angiofibroblastic degeneration of the rotator cuff tendons.[7] The subacromial bursa is rich free nerve

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endings and nociceptive agents.[8,9] Proposed cellular changes associated with intrinsic mechanisms of RCT are increased matrix metalloproteinases (MMP) and reduced tissue inhibitors of MMP. The inhibitors are tendon cell apoptosis, insulin-like growth factor (IGF-1), nitric oxide synthetase, chondroid metaplasia of the tendon and matrix changes, fatty infiltration (following tears), cytokines, and caspases. Levy *et al.* showed that subjects with acute RCT had hypovascularity in the supraspinatus tendon in comparison to hypervascularity in chronic tendinopathy. Hence, the intrinsic factors have an influence on the morphology and performance of the tendon.

The tendon normally heals with scar tissue formation. The scar tissue is rich in Type 3 collagen. Type 3 collagen has excellent elastic properties but inferior strength property. As a result scar tissue is inferior to native tendon because of the structural organization and poor matrix formation. Therefore, scar tissue must thicken to make up for its mechanical insufficiency, resulting in a stiffer tendon.

Platelet-rich plasma (PRP) is a preparation of concentrated autologous platelets containing growth factors and bioactive substances essential to musculoskeletal healing.[10-12] These growth factors are transforming growth factor β1 (TGF β1), platelet-derived growth factor, vascular endothelial growth factor (VEGF), hepatocyte growth factor, and IGF-1. These factors are biologically active and stimulate angiogenesis, epithelialization, cell differentiation, proliferation, and the formation of extracellular matrix and fibrovascular callus. PRP can be used to enhance extracellular matrix organization by enhanced cell proliferation and total collagen. *In vitro* and animal model studies suggest that PRP augments tissue healing and prevent the structural failure of the tendon in RCT by increasing tenocyte number and production of collagen (Types 1 and 3), which makes up a major portion of the tendon.[13-15]

Conservative management is the mainstay of treatment which includes relative rest, pain medication, physical therapy, and corticosteroid injections. However, many patients are refractory to standard care, and arthroscopic acromioplasty (AA) is done on those cases. Although most patients improve after AA, some fail to improve after surgery and many do not return to normal.[10] Some studies fail to show improvement after AA. PRP has been suggested as a treatment option for refractory tendinopathies including RCT.[10,16]

In case of refractory RCT, AA fails to show improvement. This leads to increasingly widespread use of PRP in clinical practice with high expectations. The aim of this prospective study is to investigate the clinical and tissue effect of coapplication PRP with AA in patients with chronic RCT. We hypothesized that PRP with AA would improve both clinical outcome and tissue characteristics.

METHODS

This was an institution-based, prospective longitudinal study. The study was conducted in our institution after getting ethical permission. All the patients were counseled about the advantages, disadvantages, and complications of the procedure. After getting written consent from patients, we performed procedure. The study period was from January 2012 to January 2015 (36 months duration).

Adult persons aged 40-70 years were recruited from a referral-based outpatient sports medicine practice. Inclusion criteria of our study were RCT with symptoms for 6 months or more, failed conservative treatment of at least 4 weeks of formal physical therapy (including rotator cuff strengthening and scapular and proprioceptive stabilization), at least one corticosteroid injection and single shoulder involvement. Exclusion criteria were joint instability, history of shoulder surgery, and corticosteroid injection within 3 months. Patients with labral lesion, complete rotator cuff tear, and adhesive capsulitis on magnetic resonance imaging (MRI) were excluded.

MRI was performed in all cases preoperatively and also on clinical follow-up period. MRI of rotator cuff was scored on a 0-5 severity scale (0: No tendinopathy; 1: Mild tendinopathy; 2: Moderate tendinopathy; 3: Moderate tendinopathy + partial thickness tear present; 4: Severe tendinopathy ± partial thickness tear present; 5: Severe tendinopathy + full thickness tear present). Patients with Grade 1 and Grade 5 were excluded from the study.

Arthroscopic procedure was done in lateral position under general anesthesia. During the procedure, shoulder joint was thoroughly examined to evaluate any other pathological condition-like labral lesion. Full thickness rotator cuff tear, frozen shoulder, or osteoarthritis and patients were withdrawn from the study. A standard AA was performed through the posterior and anterolateral portal.

PRP was prepared from the 50 ml whole blood taken from the patient. The blood was divided into five 10 ml syringes, and anticoagulant dextrose A (phosphogluconate dehydrogenase-A) solution was mixed 1:9 volume. The syringes were placed in centrifugation machine. The rotation speed and time was 3000 rpm × 3 min. It would separate red blood cell from plasma. The supernatant fluid was taken out and put in another five syringes, and 1 μg prostaglandin E1 in each syringe was mixed. The second centrifugation was performed at 4000 rpm for 15 min.

The supernatant was discarded leaving 0.65 ml in syringe, and the sediment was mixed with-it using a vortex mixer. Finally, 0.65 ml of PRP solution was prepared from 10 ml of the whole blood in the syringe. The PRP was injected into the margin of partial tear and the subacromial space.

During the arthroscopic procedure, tendon biopsy specimen was taken at baseline under general anesthesia and at the 3-month follow-up under ultrasonography guidance.

Patients were followed up at 8, 12, and 52 weeks. The primary outcome measurements were visual analog scale (VAS) score and Oxford shoulder score (OSS). Secondary outcomes included functional tests (empty can exercise with dumbbell resistance, drop arm exercise with dumbbell resistance, side-lying external rotation with dumbbell resistance, full can exercise with dumbbell resistance, external rotation at 0 and 90° with Thera-Band resistance). Bonar scoring was used for histopathological grading.

RESULTS

Demographic

About 130 patients were included in the study. Of these, 85 patients met the inclusion criteria. Among them, AA was done in 40 patients, and AA + PRP injection was given in 45 patients. The average platelet count was in 2.5 ± 3.1 AA group and 2.5 ± 3.8 in AA + PRP group. The baseline OSS in AA and AA + PRP group was 24.5 ± 3.2 and 23.6 ± 4.1, respectively. There was no statistical difference between the groups regarding demographic parameters (Table 1).

Functional Outcome

The parameters for primary outcome functional measures (VAS score and OSS) were statistically significantly improved in both groups (Table 2). The VAS and OSS were improved >95% compare to baseline. In (AA + PRP) group, the VAS and OSS were improved from 7.5 ± 0.3 and 23.6 ± 4.1 to 0.34 ± 0.2 and 48 ± 2.3, respectively. Similarly, in AA group, the VAS and OSS were significantly improved from 7.6 ± 0.3 and 24.5 ± 3.2 to 0.4 ± 0.1 and 45 ± 2.1, respectively ($P < 0.001$). Secondary functional outcome measures were also improved significantly (Table 2). The maximum effect was found in Thera-Band external rotation at 90°. The average mean was improved from baseline 33.4 ± 5.7 (AA + PRP) and 34.2 ± 4.9 (AA) to 72.3 ± 1.7 (AA + PRP) and 72.3 ± 1.7, respectively. Another parameter drop arm test also improved dramatically from 44.3 ± 7.8 (AA + PRP) and 45.3 ± 6.7 (AA) to 83.4 ± 1.5 (AA + PRP) and 83.2 ± 1.2 (AA), respectively. However, when both the groups were compared regarding primary and secondary outcome measures, there was no statistical difference (Table 3).

Table 1: Demographic parameters

Parameters	AA	AA+PRP	*P* value
Age	55.50±4.18	52.81±4.71	<0.01
Gender: Female/male	22/18	25/20	
Length of symptoms	14±1.7	13±2.1	
Baseline OSS	24.5±3.2	23.6±4.1	
Pre-operative platelet count	2.5±3.1	2.5±3.8	
Pre-operative MRI findings			
Grade 2	12	10	
Grade 3	18	22	
Grade 4	10	13	

AA: Arthroscopic acromioplasty, PRP: Platelet-rich plasma, MRI: Magnetic resonance imaging, OSS: Oxford shoulder score

MRI and Histopathology

Grade 2 MRI severity score was improved to Grade 1 in all patients in both the groups, and there was no statistical difference. In Grade 3 and Grade 4 group, there was statistically significant improvement was seen in (AA + PRP) group. Among the 22 patients, Grade 3 in (AA + PRP) group, 18 patients were improved to Grade 1. In comparison to (AA) group, where only 3 patients were improved to Grade 1 among 18 points. Similar result was found in Grade 4 in (AA + PRP) group, where among 13 patients of Grade 4 group, 11 patients were improved to Grade 1 (Table 4). According to histopathological parameters of Bonar scoring system, significant improvement was found in (AA + PRP) group (Table 5). Even after difference in histopathology, there was no difference in functional outcome measures.

There was no complication was found in both groups.

DISCUSSION

RCT is a common overuse injury in athletes and workers that occur because of the high chronic repetitive loading that surpasses the adaptive abilities of the tendon and causes micro tears and degeneration in the tendon substance. Many factors have been suspected to predispose patients to this condition by increasing the supraspinatus tendon overload. The high chronic repetitive loading stimulates the local release of cytokines, with an autocrine and paracrine modulation of cell activity that fails to adapt to continued abusive load and irritation and leads to intratendinous damage. The poor regeneration capacity of tendons, explained by the poor vascularity, oxygenation, and nutrition of this tissue, cannot cope with the applied forces and explains the low healing potential and the difficulties in the treatment of this chronic tendon disease.

In cases of injury, platelets are the first cells carried to the lesion site. In fact, they play a key role in mediating healing

Table 2: Primary and secondary outcome measurements

Parameters	Mean				*P* value
	Baseline	Week 8	Week 12	Week 52	
VAS pain (AA+PRP)	7.5±0.3	3.3±0.4	0.7±0.3	0.34±0.2	<0.001
VAS pain (AA)	7.6±0.3	3.8±0.38	0.8±0.3	0.4±0.1	<0.001
Side-lying external rotation (number of repetitions) (AA+PRP)	17.5±1.6	23.8±0.9	32.3±3.5	38.2±1.6	<0.001
Side-lying external rotation (number of repetitions) (AA)	18.1±1.5	24.7±0.7	31.3±3.6	37.5±1.2	<0.001
Empty can (sec to fatigue) (AA+PRP)	59.1±7.9	71.8±4.7	76.5±10.5	80.4±2.5	0.65
Empty can (sec to fatigue) (AA)	57.3±7.2	71.5±4.1	77.2±9.2	81.2±1.7	0.63
Drop arm (sec to fatigue) (AA+PRP)	44.3±7.8	67.7±6.5	78.2±12.5	83.4±1.5	0.002
Drop arm (sec to fatigue) (AA)	45.3±6.7	68.2±5.9	79.1±10.3	83.2±1.2	0.002
Full can exercise (no. of repetitions) (AA+PRP)	27.4±3.9	38.6±4.0	47.1±5.2	51.3±2.4	<0.001
Full can exercise (number of repetitions) (AA)	26.7±2.5	37.8±3.7	46.3±5.0	52.7±2.7	<0.001
Thera-band external rotation at 0° (s) (AA+PRP)	37.7±4.3	54.8±5.6	62.1±3.3	68.1±2.1	<0.001
Thera-band external rotation at 0° (s) (AA)	38.1±4.3	55.2±5.0	61.9±3.1	68.3±2.3	<0.001
Thera-band external rotation at 90° (s) (AA+PRP)	33.4±5.7	47.9±3.2	61.5±3.0	72.3±1.7	<0.001
Thera-band external rotation at 90° (s) (AA)	34.2±4.9	48.3±2.8	62.8±2.6	71.6±1.9	<0.001
OSS (AA+PRP)	0.23.6±4.1			48±2.3	<0.001
OSS (AA)	24.5±3.2			45±2.1	<0.001

VAS: Visual analog scale, AA: Arthroscopic acromioplasty, PRP: Platelet-rich plasma, OSS: Oxford shoulder score

Table 3: Comparison between AA and AA and PRP injection

Parameters	AA	AA+PRP	*P* value
VAS pain (0-10 points)	0.4±0.1	0.34±0.2	<0.001
Side-lying external rotation (number of repetitions)	37.5±1.2	38.2±1.6	
Empty can (sec to fatigue)	80.4±2.5	81.2±1.7	
Drop arm (sec to fatigue)	83.4±1.8	83.2±1.2	
Full can exercise (number of repetitions)	51.3±2.4	52.7±2.1	
Thera-Band external rotation at 0° (s)	68.3±2.3	68.1±2.1	
Thera-band external rotation at 90° (s)	71.6±1.9	72.3±1.7	
OSS	45±2.1	48±2.3	

AA: Arthroscopic acromioplasty, PRP: Platelet-rich plasma, OSS: Oxford shoulder score

Table 4: Comparison of MRI gradings

Parameters	AA (pts)	AA+PRP (pts)	*P* value
Grade 2	12	10	
	Grade 1-12	Grade 1-10	<0.001
Grade 3	18	22	>0.05
	Grade 2-15	Grade 1-18	
	Grade 1-3	Grade 2-4	
Grade 4	10	13	
	Grade 1-0	Grade 1-11	
	Grade 2-2	Grade 2-1	
	Grade 3-8	Grade 3-1	

AA: Arthroscopic acromioplasty, PRP: Platelet-rich plasma, MRI: Magnetic resonance imaging

Table 5: Comparison or Bonar score

Parameters	Before operative procedure	After operative procedure	*P* value
AA	9.53±1.5	7.31±1.7	>0.05
AA+PRP	9.48±1.4	2.3±1.29	

AA: Arthroscopic acromioplasty, PRP: Platelet-rich plasma

of the damaged tissue because of the capacity to release growth factors from their α-granules. Platelets are a rich source of growth factors which augment tissue healing. Among them, TGF β, VEGF, platelet-derived growth factor, IGF-1, and epidermal growth factor are important. So, PRP provides the potential for an autologous and relatively in expensive solution to facilitate tissue repair. *In vitro* studies demonstrated this mitogenic activity and that the stimulated tenocytes synthesize VEGF and hepatic growth factor, thus suggesting a beneficial effect for the treatment of tendon injuries by inducing cell proliferation and promoting the synthesis of angiogenic factors during the healing process. An animal model has also confirmed the usefulness of platelet concentrate for the treatment of tendon damage, with an increased tendon callus strength and stiffness after percutaneous injections in transacted tendons; a more rapid recovery in surgically repaired tendons has also been seen in a human study. Currently, PRP is widely used experimentally in different fields of medicine, but the evidence base for the clinical use of PRP is still in its infancy. Molloy *et al.* has applied PRP in various sports injury and concluded PRP augments tissue healing.[12] Only a few articles specifically address treatment applications in the orthopedic field and, to our knowledge, only one study has been published regarding the treatment of tendinopathy through PRP injections. Mishra treated patients affected by severe chronic tennis elbow and reported promising result, with improvement in pain and function and no complications. In delayed and nonunion of bone, it has been used with bone marrow, and the result is encouraging. Now a days, the domain has been increased and applied in spinal surgery, periodontal, and craniofacial surgery.[17,18]

The mechanism of action of PRP is not fully understood. Recently, in anterior cruciate ligament reconstruction with semimembranosus quadruple graft is used with PRP and

the tendon-bone healing on MRI is found. In partial tear of tendoachilles, retrocalcaneal tendonitis, patellar tendonitis disease, PRP injection result is encouraging. PRP has been recommended as an alternative treatment option for refractory tendinopathies including RCT.[10,16] Early clinical evidence suggests that PRP improves pain and function outcomes in some tendinopathies compared to control injection and baseline status.[19,20] One study has assessed PRP as an adjunct to arthroscopic shoulder repair, but no rigorous study has assessed PRP as primary therapy for RCT.[21]

During the study period, there was a significant improvement in VAS and OSS in both the groups. However, when both the groups were compared, there was no statistical difference both in primary and secondary outcome measurements. The results of MRI finding are encouraging and inspiring. In our study, we have found that Grade 3 and Grade 4 patients with RCT statistically significant improvement found. More than 90% patients were improved to Grade 1 (minimal tendinopathy). On MRI, complete healing of partial tear occurred in maximum patients. According to Boner staging on histopathology, there was statistically significant improvement of tendinopathy in AA + PRP group. Both these findings suggest that significantly tendon healing occurs with injection of PRP.

Our study has several limitations. First, our patients had previously received, physical therapy, corticosteroid injection, etc. PRP has not been given as the first line of treatment. Second, the sample size is small and derived from a single tertiary orthopedic center. Third, our study evaluates the result of co-application AA + PRP but not PRP alone. Fourth, a single dose and lack of knowledge of optimal dosing and concentration and also the procedure of production of PRP are the limiting factors.

CONCLUSION

Our study showed that there was significant improvement occurred in both the groups according to functional parameters. The study also concluded that significant tendon healing occurred in PRP patients according to MRI and Bonar scoring. Although there was no statistical difference was found in both groups according to functional parameters. Many aspects of rotator cuff disease are controversial, and further research is necessary in areas such as imaging, pathophysiology, and natural history to further our understanding of the disease and make improvements in diagnosis and treatment.

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