The effect of platelet-rich plasma injections in the non-surgical treatment of a partial rotator cuff tear

Julien Freitag, Ross Lenssen, Drew Slimmon, Simon Balster

ABSTRACT

Introduction: Rotator cuff tears are associated with significant morbidity and have a reported incidence of greater than 50% amongst the adult population. We present a case report of a partial rotator cuff tear treated with platelet-rich plasma injections.

Case Report: A 60-year-old female was presented with a partial supraspinatus tear having failed to improve with physiotherapy. The patient underwent a course of three platelet-rich plasma injections to her tear. Patient outcome was measured using the numerical pain rating scale (NPRS), percentage perceived improvement (PPI) and also a handheld dynamometer assessment of rotator cuff strength. Repeat ultrasound examination was performed. The patient reported improvements in pain as measured by NPRS and PPI, though maximal improvement was not maintained through to final data collection at 52nd week. Dynamometer follow-up showed improvement in strength. Ultrasound at 52nd week showed evidence of ingrowth of tissue though this did not resemble normal tendon. The patient noted increased pain post her second platelet-rich plasma injection though this was self-limiting and managed with simple analgesia.

Conclusion: In this case report, platelet-rich plasma injections for the treatment of a partial rotator cuff tear resulted in improvement in all recorded outcome measures. This highlights the need for more formal controlled trials to determine the use of platelet-rich plasma in the treatment of rotator cuff pathology.
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Keywords: Rotator cuff tear, Shoulder, Platelet-rich plasma, Pain

INTRODUCTION

Rotator cuff pathology is associated with significant morbidity and accounts for more than 4.5 million physician visits per year within the United States [1]. Incidence of rotator cuff tears has been reported as >50% amongst the adult population [2].

While surgical repair of full thickness tears show success rates of up to 85%, imaging post repair often reveals persistent cuff defects [3, 4]. This may explain recurrence of symptoms and re-tear rates reported to be as high as 57-90% [5, 6]. Furthermore, while primary surgical repair is an accepted treatment of full thickness tears there remains speculation about how best to treat symptomatic partial thickness tears.

Most classifications recognize bursal and joint surface partial rotator cuff tears. Intra-substance tears have more recently been formally described [7]. Studies have shown that bursal surface tears respond poorly to
conservative management and surgical interventions such as arthroscopic subacromial decompression, debridement and repair have all been suggested [8]. Similarly, arthroscopic follow-up of joint surface tears managed non-operatively has shown that 80% enlarge and/or progress to full thickness tears [9]. Laudicina et al. suggest that primary repair of partial tears >50% is an accepted practice, though there is no published data on its efficacy [10].

There has been growing interest in the area of biological therapies to assist musculoskeletal repair. Autologous platelet-rich plasma (PRP) is one such therapy that has gained much attention. Platelet-rich plasma is defined as a volume of the plasma fraction of whole blood having a platelet concentration above that of baseline. Several anabolic and trophic factors that participate in tissue repair processes have now been identified within PRP preparations [11]. These growth factors, including platelet derived growth factor (PDGF), transforming growth factor beta 1 (TGFβ1), insulin-like growth factor 1 (IGF1) and vascular endothelial growth factor (VEGF), have the ability to influence and direct tissue regeneration through angiogenesis, chemotaxis and cell proliferation and also effect the synthesis of extracellular matrix proteins. Platelets also release cell adhesion molecules such as fibronectin, fibrinogen and vitronectin which influence extracellular matrix synthesis and thus connective tissue development/ regeneration [12]. Recent review articles on PRP have suggested that it is being used increasingly in the clinical setting for the treatment of tendinopathy [13, 14].

Due to the significant incidence of post surgical tear recurrence, there has been considerable focus on improving long-term surgical outcome through the use of biological augmentation. The use of PRP matrices at time of surgical repair has been trialed with inconsistent results and is not widely practiced [15, 16]. Further, despite its growing use within clinical practice for the conservative management of tendinopathy there is a paucity of published data on its use in the non-surgical management of rotator cuff pathology. Kesikburun et al. have published a randomized control trial on the use of PRP in the treatment of chronic rotator cuff tendinopathy showing no improvement beyond that achieved with a traditional conservative exercise program [17]. Interestingly, however, the PRP was injected into the subacromial space and not the tendon itself. O’Donnell et al. compared intra-tendinous injections of PRP to subacromial corticosteroids and showed both significant improvement in pain and function but also a significant reduction in the later requirement for surgical repair at 12th month follow-up [18]. This result, however, may be complicated by the growing awareness that long-term outcome in tendinopathy is worse in those treated with corticosteroid injections [19].

Despite its theoretical potential in therapeutic applications within musculoskeletal medicine, trials on the use of PRP in tendon pathology have been inconclusive [20, 21]. Both the lack of uniformity in treatment protocols and differing preparation techniques have meant vastly conflicting results between publications on PRP treatments, leading to disagreement on whether PRP is an effective therapeutic modality. It is yet to be determined whether good theory equates to a successful clinical outcome.

**CASE REPORT**

**Case Presentation**

A 60-year-old female presented with gradual onset of shoulder pain with lifting and overhead activities over the last six months. She worked as an aged care assistant and had failed to improve with a physiotherapy guided scapular control and rotator cuff strengthening program. The patient had received an ultrasound-guided subacromial cortisone injection with good but, unfortunately, only short-term relief. Formal ultrasound showed evidence of a partial insertional tear of the supraspinatus tendon (Figure 1A). The physician who treated her had discussed the possibility of surgical subacromial decompression and rotator cuff repair but she was hesitant to consider surgery. Her physician referred her for consideration of autologous platelet-rich plasma (PRP) therapy.

On initial examination, the patient had normal shoulder range of motion but exhibited a painful arc from 90–180 degrees of abduction. She had pain and weakness on rotator cuff testing. Radiological examination confirmed a type I acromion, no subacromial spur and no glenohumeral osteoarthritis.

Given that the patient had failed to improve with conservative management of her partial rotator cuff tear, the trial of PRP therapy in conjunction with a continued rehabilitation program was deemed appropriate. Written information and education was provided regarding PRP and its use within tendinopathy, including relevant alternatives (i.e. surgery) and possible risks involved.

The patient underwent a course of ultrasound guided PRP injections to her insertional tear. Patient outcome was measured using the numerical pain rating scale, percentage perceived improvement and also dynamometer assessment of rotator cuff strength.

**Investigations**

Ultrasound examination prior to treatment confirmed a partial insertional supraspinatus tear (Figure 1A). Repeat ultrasound was performed at 12th month post-PRP therapy (Figure 1B).

X-ray confirmed a type I acromion, no subacromial spur and no glenohumeral osteoarthritis.
Treatment

Analysis Method

Prospective analysis of patient outcome to intratendinous PRP injection included the numerical pain rating scale (NPRS) [22], patient percentage perceived improvement (PPI) and a handheld isometric dynamometer assessment of rotator cuff strength.

NPRS was recorded prior to each injection, with follow-up intervals occurring at 6th, 17th, 25th and 52nd weeks. Percentage perceived improvement was recorded at 17th and 52nd weeks. Dynamometer testing was recorded immediately prior to the initial injection and again at 6th and 18th weeks.

Isometric dynamometer testing has been validated as a reliable assessment of rotator cuff strength and function [23–25]. Eleven isometric resisted glenohumeral tests were performed using a handheld dynamometer (Figure 2), with supraspinatus being particularly active in the ‘empty can’ and external rotation positions [26]. Every position was loaded isometrically for five seconds at a maximum tolerated contraction. Each test was performed after a demonstration so to ensure that the participant and clinician used correct technique and avoided any unwanted movements or body swaying. If a test was performed incorrectly, it was repeated to ensure it was done properly. If performed correctly, no re-test was performed as Kolber et al. have shown excellent reliability with high intra-class correlation coefficients of 0.971–0.972 [23].

Platelet-Rich Plasma Preparation

The patient received three PRP injections (weeks 0, 1 and 2).

Autologous blood (24 mL) was withdrawn from the study participant and separated into 3x8.5 mL BD Vacutainers (BD, Franklin Lakes, NJ, USA) containing ACD (trisodium citrate 22.0 g/L, citric acid 8.0 g/L, and dextrose 24.5 g/L) to prevent clotting. BD vacutainers undergo gamma irradiation to ensure internal sterility. Gamma irradiation has also been shown to reduce endotoxin expression [27]. Using a bench-top XC 2000 centrifuge the tubes were centrifuged at 1000 rpm (110×G) for 10 minutes to create a platelet-poor plasma (PPP) level, a middle buffy coat level (high in platelets and leukocytes) and a lower red blood cell layer.

Platelet-poor plasma was withdrawn from each tube to the level of the red blood cell layer and placed in a single sterile vacutainer (BD, Franklin Lakes, NJ, USA) which was re-centrifuged at 3500 rpm (1370×G) for three minutes resulting in the formation of a platelet plug and PPP. Platelet-poor plasma was withdrawn to 30 mm and discarded. The remaining PPP and platelet plug were reconstituted using gentle manual agitation resulting in leukocytes rich platelet-rich plasma medium. The PRP underwent photo-modulation using the commercial Adi-Light 2 device (AdiStem Ltd, Hong Kong). Photomodulation –polychromatic light– therapy has been
shown to increase expression of leucocyte-derived anti-inflammatory cytokines (IL-1RA) and also to cause reduction in pro-inflammatory cytokines (IL-2 and 6) [28, 29].

Inflammatory cells such as neutrophils and macrophages play an important role in the initiation of tendon/soft tissue healing through phagocytosis of degenerative/necrotic tissue [30]. Unfortunately, the presence of leukocytes can also result in a pro-inflammatory environment leading to further damage [31]. Adapting these theories to clinical practice it was decided that the injection protocol would utilize a leukocyte rich PRP preparation for the initial injection but that a five-micron filter (GVS, Bologna, Italy) would be used in the subsequent injections resulting in a leukocyte poor PRP. This protocol has not previously been described.

**Injection Method**

Under sterile conditions and ultrasound guidance, a sterile 22-gauge needle was inserted into the partial supraspinatus tear using a lateral approach. On the initial injection two milliliters of leukocytes rich PRP was injected with no concurrent use of local anesthetic. For the following two injections a five-micron filter was placed between the needle and syringe resulting in a leukocyte poor PRP preparation upon injection.

**Potential Adverse Effects**

Previous studies using PRP therapy have indicated minimal adverse effects [20, 21]. Mishra et al. documented self-limiting discomfort post intra-tendinous injections [21].

**Strengthening/Physiotherapy Program**

The patient continued the physiotherapy guided progressive strengthening program which had commenced prior to receiving PRP therapy. This program initially consisted of two low graded exercises for three sessions per day. When the patient was able to demonstrate adequate progress, the program was gradually progressed to eight more difficult exercises 1–2 sessions per day. The intensity of the exercises gradually progressed as tolerated by increasing the weight/resistance used and by altering the type of exercise to increase the lever arm/torque and to work different muscle groups. Combinations of hand weight and theraband exercises were utilised.

**RESULTS**

The NPRS gradually improved after commencing PRP treatment and reached 0 at 17th week. NPRS remained improved though had increased to three by completion of data collection at 52nd week (Figure 3).

At 17th week following the initial PRP injection, a percentage perceived improvement of 90% was reported by the patient. At 52nd week, PPI remained improved though was now only 70% (Figure 4).

Dynamometer testing (performed by the same clinician to prevent inter-examiner variability) showed progressive improvement in strength across all movements (Figures 5 and 6). Isolated supraspinatus activation in the ‘empty can’ position showed improvement of 26.93% at 6th week and 32.15% by 18th week. Loaded external rotation with elbow by side (ER at 0°) showed improvement of 32.15% by 6th week and 51.29% by 18th week. Unfortunately, dynamometer testing was not continued after 18th week due to the significant distance the patient had to travel to have this assessment.

Repeat ultrasound at 52nd week showed ingrowth of hyper-echoic tissue into the partial tear defect. This tissue did not, however, resemble tendon like structure (Figure 1B).

The patient noted a significant flare up of shoulder discomfort following the 2nd PRP injection. This was self limiting (lasting 3 days) and managed with simple analgesics (paracetamol). No other complications were noted.

**Figure 3: Numerical pain rating scale.**

**Figure 4: Patient perceived percentage improvement (PPI).**
DISCUSSION

This case study describes the use of platelet-rich plasma in the treatment of a symptomatic partial rotator cuff tear. It also documents the use of dynamometer assessment of rotator cuff strength enabling further quantitative analysis of patient response beyond that achieved with questionnaires.

Post-PRP the patient demonstrated improvement in all recorded outcome measures. NPRS improved to 0 by 17th week and remained improved — though had increased to 3 — by completion of data collection at 52nd week. The PPI was recorded as 90% at 17th week and whilst remaining improved had reduced to 70% by week 52. Dynamometer testing recorded an improvement in supraspinatus activation over 18 weeks of follow-up.

Interestingly, all values of dynamometer testing — including those not assessing supraspinatus function — improved over the course of follow-up. This supports the concept that the individual muscles of the rotator cuff work in cohesion to assist with glenohumeral control during active movement of the shoulder [32]. Unfortunately, dynamometer testing was not continued after 18th week and we do not know whether increased values of NPRS and reduced PPI would have correlated with reduction in dynamometer values.

Repeat ultrasound at 52nd week showed development of tissue ingrowth into the tear though this did not resemble tendon tissue. This imperfect healing response perhaps explains why the patient, after an initial significant improvement in NPRS and PPI, showed some regression in these values by week 52. This highlights the difficulty in assessing PRP as an adjuvant biological therapy in tendon pathology. The protocol used in the case study involved three injections of PRP at weekly intervals. It is accepted that tendon healing occurs in 3 overlapping phases of inflammation, proliferation and remodeling [33]. As the remodeling phase may extend over 12 months it is conceivable that further injections of PRP are required to stimulate a more appropriate healing response.

Further, this case study uses a PRP preparation method that is not common to all published research and its use of a five-micron filter to create a leukocyte poor PRP has not to our knowledge been previously published in literature. The injection protocol and PRP preparation all add to a treatment ‘recipe’ with significant possible variables that will influence the outcome. This lack of ‘recipe’ uniformity makes it difficult to compare research papers on PRP. DeLong et al. have suggested the use of a PAW classification system (platelet count, activated versus inactivated, presence or absence of white blood cells) to enable formal comparison of PRP publications and this should be adopted if a more controlled trial/study was performed [34].

The complex nature of rotator cuff pathology is another area that may influence the effectiveness of biological therapies such as PRP. Understandably, it is questionable whether the results of this study would have reliable external validity if used for other patients with similar but not exactly the same pathology. It is unlikely that PRP would be beneficial for under-surface/joint or top-surface/bursal partial thickness rotator cuff tears where there is no contained defect in which to inject PRP.

Despite the aforementioned protocol and tendon pathology variables, and whilst recognizing the low level of evidence, the results of this case study indicate that in a well-selected patient population, PRP may assist in the non-surgical management of partial rotator cuff tears. Further investigation with an appropriately powered randomized control trial is needed to confirm the external validity of this treatment and use within clinical practice.
CONCLUSION

Partial rotator cuff tears are a cause of significant shoulder disability. Surgical repair of rotator cuff tears are complicated by significant re-tear rates and recurrence of symptoms. The use of platelet-rich plasma in partial rotator cuff tears may offer a non-surgical treatment for patients who do not respond to conservative rehabilitation methods. Platelet-rich plasma is an autologous medium that offers promise in the treatment of tendinopathies yet current evidence is inconclusive and further controlled research is needed.

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Author Contributions

Julien Freitag – Conception and design, acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Ross Lenssen – Acquisition of data, Analysis and interpretation of data, Critical revision of the article, Final approval of the version to be published

Drew Slimmon – Acquisition of data, Critical revision of the article, Final approval of the version to be published

Simon Balster – Acquisition of data, Critical revision of the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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