Platelet Rich Plasma as a Treatment Method for Rotator Cuff Tears

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Abstract

The prevalence of the rotator cuff (RC) tears is ~21% in the general population, with higher incidences in individuals over 50. Irrespective of surgical repair techniques employed, re-tear rates are alarmingly high, indicating the need for improvement to the current treatment methods. A method that has recently increased in popularity is the administration of platelet-rich-plasma (PRP), as it has been proposed to significantly encourage and improve healing in a plethora of musculoskeletal tissues, although experimental conditions and results are often variable. This review aims to critically evaluate current literature concerning the use of PRP, specifically for the treatment of RC tears. There are ongoing conflicts debating the effectiveness of PRP to treat RC tears; with literature both in favour and against its use either having profound methodological weaknesses and/or limited applicability to most individuals with RC tears. There are numerous factors that may influence effectiveness, including the subgroup of patients studied and the timing and method of PRP delivery. Thus, in order to ascertain the clinical effectiveness of PRP for RC tears, the preparation protocol and composition of PRP must be standardised, so an accurate assessment and comparisons can be undertaken. Prior to clinical realisation, there is a requirement for a defined, standardised, quality-controlled protocol/procedure considering composition/formulation (of PRP); injury severity, dosage, frequency, timings, controls used, patient group, and rehabilitation programmes. Nevertheless, it is concluded that the initial step to aid the progression of PRP to treat RC tears is to standardise its preparation and delivery.

Keywords Musculoskeletal injury · Platelet-rich plasma · Standardisation · Re-tear · Rotator cuff tear

Introduction

Rotator cuff (RC) tears (Fig. 1) are one of the most common causes of shoulder pain, usually leading to difficulty sleeping and poor function [1–3]. The prevalence of RC tears is approximately 21% in the general population, which increases with age [4–7]; with considerably more tears sustained by

individuals aged 50 and older [8]. RC tear risk factors include degenerative changes to the tendon, traumatic injury, genetic predisposition and repetitive shoulder impingement [4, 9–11]. Both non-operative [12, 13] and operative treatments/therapies [14] can be used for RC tears, with detailed studies published comparing which strategy is the most effective [15, 16], but surgery may often be the only option for some patient subgroups. Despite advancements in surgical techniques, there is still an alarming tendon re-tear rate, ranging from 15 to 40% regardless of the surgical technique employed [1, 17, 18]. Therefore, operative methods of treating RC tears require significant optimisation to reduce secondary re-tears.

The volume of research aimed at improving clinical outcomes post-surgery has increased considerably in recent years, leading to advances in surgical methods and techniques, along with enhancements in rehabilitation programmes [19–21]. For instance, a recent development has been the increasing use of platelet-rich plasma (PRP) as a novel method of treatment for musculoskeletal injuries. Sengodan et al. (2017) suggested that PRP can reduce the pain caused by tendon tears, while accelerating the healing process and lessening extensive rehabilitation time [22]. PRP theoretically

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Fig. 1 Healthy shoulder, small RC tear, medium-large RC tear, complete RC rupture (large tear)

accelerates tendon healing by increasing revascularisation at the injury site. It is widely understood that PRP contains a high concentration of platelets, which are a rich source of numerous types of growth factors with restorative properties [22–25]. Numerous clinical studies have discovered that PRP enhanced RC tear repair and concluded that PRP has the potential to improve standard RC tear repair methods [26–28]. Conversely, many clinicians do not support the use of PRP in RC repair, as it failed to improve the RC healing process or re-tear rates when compared with control patients [29]. Furthermore, Carr et al. (2015) claimed that PRP may even have a detrimental long-term effect on the structural properties of the tendon [30]. Thus, the aim of this narrative review is to critically evaluate the literature to assess the effectiveness of PRP as a treatment method for RC tears in order to provide explanations for the frequent conflicting findings within published studies.

PRP Preparation Methods and Composition

In general, PRP preparation involves the collection of 20–60 mL of blood from the patient; anticoagulant is then added prior to centrifugation using a two-step process in order to concentrate and separate out the platelets [31]; 2–6 mL of PRP is extracted and activated using agents such as thrombin to induce the release of platelet growth factors and polymerisation of fibrinogen into fibrin [32], followed by an injection of the concentrated PRP into the patient [33].

Chahla et al. (2017) conducted a systematic review into the composition and preparation protocols of PRP in 105 different clinical studies when used to treat musculoskeletal conditions [34]. It was revealed that just 10% of the published studies provided enough information regarding the preparation protocol that would enable their methods to be repeated. Also, only 16% of studies reported sufficient information on the composition of the PRP samples. Thus, despite the widespread use of PRP, inadequate information is provided regarding PRP preparation protocol and formulations. Confusion regarding the

terminology used to define, classify, and describe variations in platelet concentrations further exacerbates the variation and apparent lack of quality controls in reported protocols. Thus, Ehrenfest et al. (2009) proposed four families of PRP based upon cell content and fibrin architecture [35] (Table 1). However, there is still a requirement for the development of standardised PRP preparation protocol, and composition is essential for assessing its effectiveness as a treatment for musculoskeletal conditions [34, 36, 37]. Standardisation would also enable direct comparisons between studies to be made and successful studies to be reproduced with ease if required. Standardisation of the protocol and composition of PRP would allow researchers to determine whether PRP is an integral component of the treatment for RC tears, which currently remains controversial.

Discussion

PRP Treatment for RC Tears

PRP is increasingly used in a clinical environment since it enables the localised delivery of cellular and humeral mediators that accelerate the healing process [38]. Chahla et al. (2017) proposed that lenient regulations for the clinical administration of PRP are a potential cause of its recent rise in popularity within musculoskeletal medicine [34], including the management of knee osteoarthritis [33].

Despite these leniencies, the optimal dose range of PRP is yet to be established [39]. A possible explanation for this could be that there is a considerable amount of individual variation in the blood concentration of platelets and growth factors [40, 41]. Furthermore, there are both surgical- and patient-specific factors that may affect RC healing that have been previously reviewed by Menon et al. (2019). These include RC chronicity, co-morbidities, previous repair techniques employed, suturing techniques, follow-up and post-operative rehabilitation; patient age and lifestyle (risk factors include smoking, high cholesterol, and diabetes). An

Table 1 Four categories of PRP based on cell content and fibrin architecture

PRP classification	Content
Pure platelet-rich plasma (P-PRP)	No leucocytes Low-density fibrin network Injectable formulation
Leucocyte- and platelet-rich plasma (L-PRP)	Contains leucocytes Low-density fibrin network Injectable formulation
Pure platelet-rich fibrin (P-PRF)	No leucocytes High-density fibrin network Gel formulation, non-injectable
Leucocyte and platelet-rich fibrin (L-PRF)	Contains leucocytes High-density fibrin network Injectable formulation

additional factor that needs addressing is the difference in the preparation protocol of PRP which make it difficult to directly compare individual studies and to definitively assess the influence of PRP on the healing process [42]. This may provide a legitimate explanation for the conflicting findings within the literature regarding PRP as an effective treatment method for RC tears.

Critique of the Clinical Effectiveness of PRP for Treatment of RC Tears

Researchers and clinicians are currently divided as to whether PRP should be involved in RC tear treatment, with conflicting clinical outcomes published in the literature. The reported benefits and potential detrimental effects of PRP will be discussed in the following sections.

Favourable Benefits of PRP for RC Healing

PRP is attractive in that it offers an alternative to conventional surgery corticosteroid injections [43] and/or in instances where conservative treatments have failed. The proposed role of PRP is to decrease pain and inflammation while stimulating healing [44]. Although the exact mechanism remains unclear, it has been theorised that the release of growth factors in combination with high concentrations of activated platelets stimulates and promotes muscle and tendon healing and growth [45, 46]. In some instances, the benefit has been reported to be cost-effective with prolonged pain management and lower risk of adverse side effects compared with conventional treatments [22].

Rha et al. (2013) conducted an investigation comparing the effects of PRP injections with dry needling treatment in 39 patients with either supraspinatus tendinosis or a tear smaller than 1.0 cm [47]. Dry needling refers to a technique which utilises thin monofilament needles which are inserted without

the use of injectate; although often associated with intramuscular pain, it can also be applied to the ligaments, tendons, fascia, scar tissue, neurovascular bundles, and within the vicinity of peripheral nerves to manage pain [48]. The study reported that the PRP injections were more effective at reducing pain and disability compared with dry needling. The advantageous impact of PRP-treated supraspinati was reported to be still evident 6 months following the procedure, indicating that PRP injections are a safe and suitable prolonged treatment method of treating RC injury, at least for the management of small RC tears.

More recently, Jo et al. (2015) demonstrated that PRP treatment can improve the quality of the repair in patients with medium or large RC tears (Fig. 1). This was supported by a significantly lower re-tear rate ($P = 0.032$) and increased cross-sectional area of the supraspinatus ($P = 0.014$) in the PRP-augmented repair group when compared with a conventional treated group [49]. However, no significant differences in healing rate, flexibility, muscle strength, function, and pain scores between groups were identified.

Sengodan et al. (2017), however, did confirm a reduction in patient pain scores with improved shoulder function at 8 and 3 months following treatment with ultrasound guided PRP injections. As the authors indicated, there were many strengths of this investigation, including that function and pain scores were obtained at frequent time intervals and an impressively high follow-up rate of 91% was seen at 8 weeks. However, it should be noted that the follow-up time period of 8 weeks is relatively short when compared with similar studies and was arguably too short to assess the prolonged effectiveness of PRP injections for RC repair.

Unfavourable Effects of PRP for RC Healing

Despite the reported aforementioned benefits of PRP, the evidence is predominantly anecdotal and/or lacking scientific

rigour and the majority of authors are unable to report significant advantages in randomised clinical trials with more prolonged follow-up periods [50]. In a recent meta-analysis, Fu et al. (2017) concluded that no difference in pain and disability outcomes could be distinguished when comparing patients treated using PRP or a platelet-rich fibrin matrix and those who were treated conventionally [51]. However, only a small number of studies were included in the analysis and a wide variation between studies was evident [51]. This ultimately reduced the power the analysis provided. The authors acknowledged this and conceded that the pain scores included in the summary of PRP's effectiveness may not correlate with the severity of the RC tear, thus limiting the conclusions drawn.

Akin to Fu et al. (2017), Charousset et al. (2014) also reported no difference in tendon healing quality between patients who had leucocyte-PRP injections during their arthroscopic repair of large RC tears and those that did not based on magnetic resonance imaging (MRI) evaluations [52]. The authors do acknowledge that a reduced re-tear rate has been discovered in PRP-treated patients with small and medium tears in previous investigations [53]. Similarly, Castricini et al. (2011) failed to establish any enhancements in the healing of small or medium RC tears treated arthroscopically with the administration of PRP [54]. These studies indicate the complexity of encountering definitive clinical evidence on the value of PRP in enabling an improved recovery from RC tears. Further clinical trials utilising PRP specifically for RC injuries are presented in Table 2 (modified from Dickinson and Wilson 2018 [28]).

As formerly mentioned, PRP may potentially have a negative long-term impact on tendon structure that increases tear susceptibility [30]. Carr et al. (2015) investigated the clinical and tissue effects following the co-application of PRP injection with arthroscopic acromioplasty compared with arthroscopic acromioplasty alone. It was reported that the co-application had no significant clinical benefit and most significantly detrimentally altered the tendon tissue and cellular properties. However, this study was conducted solely on patients with chronic symptoms that had previously failed to respond to conservative treatments prior to the study [30]. Furthermore, the mean age of the patients was 52.2 years. Another limitation of this study is that there were variations in the preparation of PRP and compositions which ultimately make the clinical benefit of PRP difficult to compare between patients. Carr et al. (2015) acknowledged that the absence of a well-established optimal dose for PRP did limit the power of their study. Therefore, the interpretation made by the authors that PRP has a detrimental effect on RC repair and tendon structure may be somewhat biased, as the treatment was less likely to succeed in this particular subgroup of patients.

Factors Influencing the Outcome of PRP Treatments

There are a plethora of explanations that may influence the effectiveness of PRP as a treatment for RC tears that may partially explain the opposing evidence presented in published studies. Bergeson et al. (2012) proposed that PRP concentrations and delivery, along with the subgroups of patients studied, are factors which if optimised could lead to considerable clinical enhancements [29]. For example, repeat administrations and the use of scaffolds for sustained delivery of PRP may inevitably provide more benefits compared with a single dose for more serious RC tears. Charousset et al. (2014) advocated that additional PRP injections 3 weeks into the recovery period may improve RC tendon healing efficiency as this was the case for chronic tendinopathies in past studies [52]. Additionally, Barber et al. (2011) concluded that using two PRP fibrin matrices instead of one led to a decline in RC re-tear rate based on MRI data [61]. Therefore, these studies reiterate that PRP concentrations and the timing of its administration are likely to have a major impact on the success of PRP treatment for RC tears.

Barber et al. (2011) highlighted the substantial disparities in PRP preparation methods; these include the type of anticoagulants used and whether leucocytes are included [61]. The presence of leucocytes has been well debated among researchers as it has formerly been recognised that PRP products without leucocytes are less effective at preventing infections developing at the injury site [29]. It has also been proposed that the addition of leucocytes to PRP could have a negative effect on healing as there will be more neutrophils present in the RC, leading to the production of more reactive oxygen species that kill both healthy and injured cells. The inclusion or exclusion of leucocytes in PRP seems to have a large bearing on its effectiveness regardless of the potential reduction in infection risk or the damaging consequences of neutrophils [62–65]. Given these inconsistent preparation approaches and compositions for PRP, further investigations are essential so that the optimal methods and concentrations can be established for the use of PRP to treat RC tears.

Conclusion

Advancements in RC tear treatment are required imminently as the current re-tear rate is alarmingly high. PRP administration has shown promise in enhancing RC tear healing in numerous studies, although drawbacks of these studies have been well documented in this review. To accurately assess PRP's effect on the healing of RC tears, future research should aim to standardise PRP's preparation and composition. The factors identified are likely to also have a bearing on the clinical efficacy of PRP. Prior to clinical realisation, there is a requirement for a defined, standardised, quality-controlled

Table 2 Comparison of clinical studies utilising PRP for RC injuries, modified from Dickinson and Wilson, 2018, [28])

Reference	Injury type	Intervention	Control	Significant findings/PRP benefit
Pandey et al., 2016 [55]	Medium and large degenerative posterolateral tears	Surgery & PRP (<i>n</i> = 52)	Surgery alone (<i>n</i> = 50)	VAS ↓ @ 1,3 and 6 months Constant-Murley score ↑ @ 12 and 24 months UCLA ↑ at 6 and 12 months Re-tear rate ↓ @ 24 months (only for large tears). Ultrasound - ↑ vascularisation @ 3 months
Carr et al., 2015 [30]	Rotator cuff tendinopathy	Treatment group (<i>n</i> = 25) received surgery + PRP	Surgery alone (<i>n</i> = 23)	–
Jo et al., 2015 [49]	Medium to large tears	PRP-augmented repair (<i>n</i> = 37)	Conventional repair (<i>n</i> = 37)	Re-tear rate ↓
Malvota et al., 2014 [50]	Complete supraspinatus tears	Surgery and PRP with autologous thrombin (<i>n</i> = 27)	Surgery alone (<i>n</i> = 27)	–
Antuña et al., 2013 [56]	Massive rotator cuff tear	Treatment group (<i>n</i> = 14) received 6 mL PRF (Vivostat®)	Surgery alone (<i>n</i> = 14)	Constant score ↑ @ 1 year VAS ↓ MRI – 10/14 PRF group had re-tear
Kesikburun et al., 2013 [57]	Chronic rotator cuff tendinopathy	PRP group (<i>n</i> = 20)	Placebo group (<i>n</i> = 20)	–
Rodeo et al., 2012 [58]	Rotator cuff tear	Surgery and received PRFM at tendon-bone interface (<i>n</i> = 40)	Surgery alone (<i>n</i> = 39)	–
Weber et al., 2013 [59]	Rotator cuff tear	Platelet rich fibrin-matrix (<i>n</i> = 30)	No treatment control group (<i>n</i> = 30)	–
Randelli et al., 2014 [60]	Complete rotator cuff tear	PRP and autologous thrombin component (<i>n</i> = 26)	No treatments (<i>n</i> = 27)	Pain ↓ @ 3,7,14, and 30 weeks UCLA and external rotation strength ↑ @ 3 months. SER ↑ 2 years post-op

PRP platelet-rich plasma; PRF platelet-rich fibrin; PRFM platelet-rich fibrin matrix; VAS visual analogue scale (pain); UCLA = University of California, Los Angeles; “–” indicates no significant functional or clinical benefit of PRP treatment

protocol/procedure considering composition/formulation (of PRP); injury severity, dosage, frequency, timings, controls used, rehabilitation programmes, and patient groups. Thus, in addition to protocol standardisation, patient inclusion and exclusion criteria including age, injury type, severity, and comorbidities need consideration. Only then can we definitively resolve whether PRP aids the healing of RC tears. If future investigations confirm PRP’s usefulness, then research can be initiated to determine the optimum preparation methods and composition.

Unfortunately, the existing evidence researchers are basing their conclusions on is somewhat bias or has limited applicability to the majority of patient subgroups. Nevertheless, it is concluded that the initial step to aid the progression of PRP to treat RC tears is to standardise its preparation and use.

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Compliance with Ethical Standards

Conflict of Interest All authors declare that they have no conflict of interest, commercial, or of other association.

Ethical Approval This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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