

Platelet rich plasma in treating tendinopathies

By

WorkSafeBC Evidence-Based Practice Group

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About this report

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The Evidence-Based Practice Group was established to address the many medical and policy issues that WorkSafeBC officers deal with on a regular basis. Members apply established techniques of critical appraisal and evidence-based review of topics solicited from both WorkSafeBC staff and other interested parties such as surgeons, medical specialists, and rehabilitation providers.

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Background

Even though the concept of using growth factors contained in activated platelets to help heal wounds dated back to the early 1980s, it is relatively recently that the use of platelet rich plasma (PRP) in treating various musculoskeletal disorders has become more prominent.^{1,9} Laboratory studies have demonstrated that autologous platelet concentrates contain high concentrations of bioactive factors that may be beneficial for tissue healing and regeneration.^{1,6,9} The different bioactive factors which are released upon platelet activation include platelet-derived growth factor (PDGF), transforming growth factor (TGF), vascular endothelial growth factor (VEGF), insulin-like growth factor (IGF) and epidermal growth factor (EGF).^{1,6} These proteins are considered to be histo-promotive factors, hence they may influence tissue healing through processes including cellular chemotaxis, proliferation and differentiation, removal of tissue debris, angiogenesis, and the laying down of extracellular matrix.¹ However, studies to date suggest that there is still no consensus on what the crucial elements of PRP are. It remains unclear how PRP produces, if any, effects on inflammation, proliferation, and remodelling in wound and tissue healing. Optimal methods for producing this concentrate are also parameters in PRP production that have not been standardized.^{1,6,9,14} With regard to the role of PRP in treating tendon injuries, experts state that even though there is some evidence that the *in vivo* application of PRP in tendon injuries might accelerate the catabolic demarcation of traumatically injured tendon matrices and promote angiogenesis and formation of fibrovascular callus, whether this process would also be beneficial for tendinopathies, which are degenerative in nature, remains to be elucidated.⁶

The objective of this short systematic review is to investigate the efficacy/effectiveness of PRP in treating tendinopathies.

Methods

- Systematic literature searching was conducted on April 22, 2009.
- Searching was conducted on commercial medical literature databases including Ovid MEDLINE Daily Update, Ovid MEDLINE, EMBASE and BIOSIS Previews, that are available through the OvidSP Interface.
- A combination of keywords were employed in searching. These keywords included: (tendonitis OR tendinitis OR myofasciitis OR epicondylitis OR tendinopathy OR tendinopathies) AND ((platelet-rich plasma) OR (platelet rich plasma) OR (plasma-rich growth factor\$) OR (plasma rich growth factor\$) OR (autologous platelet gel\$) OR (autologous platelet concentrate\$)). Search results were limited to studies conducted in human subjects.
- Eleven²⁻¹² studies were identified through searching. Upon examination of the titles and abstracts of these studies, five^{3,5,8,9,12} studies were retrieved in full for further appraisal.

- Manual searching through the references of these studies^{3,5,8,9,12} was also conducted. This searching identified six^{1,13-17} more articles which were also retrieved.

Results

Of the eleven articles^{1, 3,5,8,9,12-17} fully retrieved, seven^{1, 3,5,8,9,16,17} were excluded as they were in the form of expert reviews, did not provide primary data, or studied the injection of whole blood as opposed to concentrated platelet. Four studies¹²⁻¹⁵ were thought to be relevant, and were appraised further and are discussed below.

- Volpi et al.¹² reported the outcomes of the application of PRP to eight athletes (Level of evidence 5. Appendix 1) considering surgical intervention for chronic patellar tendinosis recalcitrant to conservative treatments. Aside from a single injection of PRP, patients also received individualized rehabilitation protocols. It is not clear whether patients received additional interventions such as analgesics. At 120 days post injection, Volpi et al. reported that seven patients (one drop out) reported on average VISA scores of 75.0 compared to VISA scores of 39.25 pre injection. *The outcome of this very small case series needs to be interpreted with caution since it is not clear how these patients were selected and the contribution of co-interventions cannot be discounted. The VISA (Victorian Institute of Sport Assessment) scale was developed to assess symptoms, simple tests of function, and the ability of patients to undertake sports.*
- Another small case series (Level of evidence 5. Appendix 1) by Randelli et al.¹³ reported the outcome of the application of PRP during arthroscopic rotator cuff repair. Fourteen patients underwent arthroscopic rotator cuff repair, were injected with autologous PRP and autologous thrombin component after tear repair, and were instructed to follow a standardized rehabilitation protocol. At 24 months post operation, 13 patients showed an average of 4.6 point decrease in their 0 to 10 visual analog scale pain score, 16 point increase in their subjective UCLA Shoulder rating scale, and 30 point increase in their Constant-Murley Shoulder Outcome score. *The fact that there was no control in this case series makes it very difficult to assess the contribution of PRP, if any, in the outcomes of arthroscopic rotator cuff repair.*
- In a small case-control study (Level of evidence 3. Appendix 1), Sanches et al. investigated the outcomes of application of PRP during Achilles tendon surgery in promoting healing and functional recovery. Twelve athletes who underwent open suture repair due to complete Achilles tendon tear were conveniently assigned, on a 1:1 ratio, to either receive (6 patients) or not receive PRP (6 patients) post surgery. The authors concluded that athletes receiving PRP recovered their range of motion earlier (7 weeks vs. 11 weeks), showed no wound complications, and took less time to take up gentle running (11 weeks vs. 18 weeks). *Aside from the limitations of the size of the sample in this study, it should be noted that there was an imbalance of potential confounders (e.g. age) between cases and controls which were not taken into account in the data analysis of this study; blinding, which may reduce potential*

measurement bias, was not implemented; and it is not clear how cases and controls were recruited. Further, this study provides evidence on the wide range of the concentration of platelets when using the same centrifugation method.

- Mishra and Pavelko¹⁵ reported a study which was started/planned as a small case-control (Level of evidence 3. Appendix 1) but ended up as a small case series (Level of evidence 5. Appendix 1) due to drop-outs. (*Strangely, the journal classified this study as a cohort study with level of evidence 2*). The authors compared the efficacy of PRP (n=15) and bupivacaine (n=5) in treating chronic elbow tendinosis. Eight weeks post injection the PRP patients reported 60% improvement in visual analogue scale (VAS) pain score compared to 16% improvement in bupivacaine (control) patients. After eight weeks, three (out of five) control patients withdrew from the study and were not reported on further. At six months post injection, cases reported 81% improvement in their VAS pain score and at final follow-up (*the duration considered as final follow-up varied among cases from 12 to 38 months post injection*) PRP patients reported 93% reduction in their VAS pain score. *It should be noted that there was an imbalance in potential confounders, such as age and duration of pain, between PRP and bupivacaine-injected patients at the beginning of the study which was not taken into account in the reporting of outcomes. It should also be noted that potential selection bias cannot be discounted due to the high drop-out rate.*

Summary/Conclusion

- Tendon healing is a complex process in which many growth factors are involved, and their respective roles still need to be elucidated.
- There is some laboratory evidence that PRP contains a higher concentration of these growth factors that may play significant roles in tissue healing, including tendon healing, especially in traumatic tendon disruption.
- There is also some evidence showing the level/concentration of these growth factors in PRP varies depending on the protocol and the devices used to spin the blood.
- To date, with regard to the efficacy/effectiveness of PRP in treating tendinopathies in humans, there is some low quality and low level evidence on the efficacy of PRP in treating tendinopathies.

Postscript

This rapid systematic review was rewritten, on April 8, 2010, from its original email version into this format. Between April 2009, when the literature search was conducted, and April 2010, a high quality randomized controlled trial (Level of evidence 1. Appendix 1) was published investigating the efficacy of PRP in treating chronic Achilles tendinopathy. In a randomized controlled trial of 54 patients diagnosed with chronic Achilles tendinopathy, de Vos et al.¹⁸ reported that, at 24 weeks post intervention, among patients treated with eccentric exercises, a

PRP injection did not result in significant improvement in pain and activity compared to saline injection as measured by the Victorian Institute of Sports Assessment – Achilles score. *To date, this RCT by de Vos et al. provides perhaps the best available evidence on the efficacy of PRP in treating tendinopathy.*

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Appendix 1

WorkSafeBC Evidence-Based Practice Group levels of evidence ^{adapted from 1,2,3,4}

1	Evidence from at least 1 properly randomized controlled trial (RCT) or systematic review of RCTs.
2	Evidence from well-designed controlled trials without randomization or systematic reviews of observational studies.
3	Evidence from well-designed cohort or case-control analytic studies, preferably from more than 1 centre or research group.
4	Evidence from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments could also be included here.
5	Opinions of respected authorities, based on clinical experience, descriptive studies or reports of expert committees.

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