

Cochrane Corner



Are autologous whole blood or platelet-rich plasma (PRP) injection effective and safe for lateral elbow pain? - A Cochrane Review summary with commentary

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The aim of this commentary is to discuss in a rehabilitation perspective the Cochrane Review "Autologous blood and platelet-rich plasma injection therapy for lateral elbow pain"¹ by Karjalainen TV et al.¹, published by Cochrane Musculoskeletal. This Cochrane Corner is produced in agreement with Journal of Musculoskeletal and Neuronal Interactions by Cochrane Rehabilitation with views* of the review summary author in the "implications for practice" section.

Background

Lateral elbow pain is an umbrella term that includes several conditions such as Tennis Elbow, Lateral Epicondylitis and Lateral Humeral Epicondylitis. It is a prevalent condition that affects men and women equally, mainly over 40 years old. Overall prevalence estimated is about 1-3% and an incidence of 4-7 per 1000 people a year, representing two-thirds of elbow pain in general practice². Pathogenesis is associated with an overuse of extensor carpi radialis

brevis causing an inflammation, called enthesitis, that is histologically characterized by fibroblast proliferation, vascular hyperplasia, and disorganization of collagen fibrils. Patients usually complain of tenderness over the common extensor origin at the lateral epicondyle that worsened with active movement, in particular during resisted dorsiflexion of the wrist and middle finger. Clinical features and examinations usually allow the formulation of a proper diagnosis. Pharmacological approaches including topical and oral nonsteroidal anti-inflammatory drugs are commonly used³, while rehabilitation therapies such as stretching, and progressive resistance exercises in association with physical therapy modalities are often administered (e.g. ultrasonography, iontophoresis, extracorporeal shock wave therapy, laser therapy)⁴. Among invasive procedures, local corticosteroid injection is a technique that seems to provide a significant reduction of pain in a short-term period⁵. Recently, autologous whole blood and platelet-rich plasma (PRP) are injected into affected tendons. Indeed, considering pathophysiological and histological features involved in

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¹ This summary is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2021, Issue 9, Art. No.: CD010951, DOI: 10.1002/14651858.CD010951.pub2 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

* The views expressed in the summary with commentary are those of the Cochrane Corner author (different than the original Cochrane Review authors) and do not represent the Cochrane Library or Wiley.



lateral elbow pain, these interventions could have a putative role in the regeneration and healing of involved tendons. However, their role in the management of lateral elbow pain still remains unclear.

Autologous blood and platelet-rich plasma injection therapy for lateral elbow pain

(Karjalainen TV, Silagy M, O'Bryan E, Johnston RV, Cyril S, Buchbinder R, 2021)

What is the aim of this Cochrane review?

The aim of this Cochrane Review was to evaluate the benefit and safety of autologous whole blood or platelet-rich plasma (PRP) injection for treatment of lateral elbow pain.

What was studied in the Cochrane review?

The population addressed in this review were adults (>16 years) with lateral elbow pain that is reproduced by palpation, increased by dorsiflexion of wrist, second and third finger and may have included ultrasound or magnetic resonance imaging showing focal hypo-echoic areas, tears or alterations in the fibrillary pattern in the common extensor tendon origin.

Interventions studied were the injection of autologous whole blood, PRP, or other autologous blood products in lateral elbow. Comparisons were placebo, no treatment, physical therapy (including exercise, use of brace/orthotic), other agents (glucocorticoid injection, hyaluronic acid injection, stem cell therapy), surgery, pharmacological intervention and supplements. Major outcomes analyzed were participant-reported pain relief (considered as reduction of pain of 30% or greater, or 50% or greater), mean pain (visual analogue scale or a numerical rating scale, or as a function question sub-score), function and disability (Patient-Rated Tennis Elbow Evaluation (PRTEE) or Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire), participant's perception of overall effect or success (Patient Global Impression of Change (PGIC) scale), health-related quality of life (Short Form-36 (SF-36), withdrawals due to adverse events and of participants with adverse events.

Search methodology and up-to-dateness of the Cochrane review?

The review authors searched for studies that had been published up to 18 September 2020 in several database, including Cochrane Central Register of Controlled Trials (CENTRAL) (via Ovid), Medline, Embase, ClinicalTrials.gov and World Health Organization International Clinical Trials Registry Platform. Authors searched for trials and reviewed potentially relevant articles for inclusion in the review.

What are the main results of the Cochrane review?

The review included 32 studies, thirty studies were RCTs and two were quasi-randomised trials. Twenty-five studies

had two intervention arms, and seven had three intervention arms. A total of 2337 participants ranging from 25 to 230 subjects per trial received autologous blood or PRP. Most of patients were female (56%) and the mean age of participants ranged from 36 to 53 years. Most of trials compared PRP to glucocorticoid injection (15 trials). Only four trials used rehabilitative intervention versus autologous blood or PRP injection (two trials with tennis elbow orthosis and exercise, one trial with Extracorporeal Shock Wave Therapy-ESWT, and one trial with laser therapy).

The review showed that, compared to placebo, both PRP and autologous blood injections at three months follow-up:

- probably provide little to no benefit for pain measured on a 0 to 10 scale, where 0 is no pain (mean pain was 0.16 points better, 95% CI, 0.29 worse to 0.60 better, 8 studies, 523 participants; moderate certainty of the evidence)
- probably provides little to no benefit for function measured on 0 to 100 scale, where 0 is best function (mean function was 1.86 points better, 95% CI, 1.25 worse to 4.97 better, 8 studies, 502 participants; moderate certainty of the evidence)
- it is uncertain whether PRP provides better treatment success (considered as an improvement of 25% for pain or function) than placebo, (RR 1.0; 0.83 to 1.19, 4 studies, 372 participants, very low certainty of evidence)
- may not increase the number of people reporting adverse events (RR 1.14; 0.76 to 1.72, 5 studies, 425 participants, low certainty of evidence)
- it is uncertain whether PRP results in more people withdrawing due to adverse events (RR 0.32; 0.03 to 2.92, 1 study, 80 participants; very low-certainty evidence)

What did the authors conclude?

The authors concluded that, compared to placebo, autologous blood and PRP probably make little or no difference in improving pain and function. Moreover, it is uncertain whether these interventions improve treatment success or increase withdrawals due to adverse events. Although, these interventions did not increase the risk of adverse events compared with placebo there is a small risk of infection and pain related to injection therapies.

What are the implications of the Cochrane evidence for practice in rehabilitation?

Lateral elbow pain is a condition that is commonly associated with repetitive occupational or athletic activities involving wrist extension and supination. People usually complain of severe limitation of arm function and reduced health-related quality of life⁶. Among non-surgical strategies, several types of injections have been used in clinical practice. Steroids injections have been commonly used for the treatment of tennis elbow, with significant short-term effects mainly on pain. Hyaluronic acid injection also seems to improve pain similar to steroids but with longer effect up to 1 year⁷. However, these benefits seem to be greater in patients with moderate epicondylitis. Recently, new agents are proposed for injection administration, e.g.

PRP and autologous whole blood. Platelet-rich plasma is developed by centrifuging a patient's blood and isolating platelet-rich fraction. It contains high levels of various growth factors including platelet-derived growth factor, TGF- β , and VEGF. Whereas autologous blood involves collection of the patient's blood, which is then injected directly into the elbow. The supposed biological effect of PRP is to deliver platelets that would release high concentrations of platelet-derived growth factors that induce fibroblastic mitosis, and stimulate angiogenesis and healing of the affected tendons⁸.

This review investigated the benefits of autologous blood and PRP for lateral elbow pain with regard to pain relief, function, patient satisfaction and quality of life. However, the results of this review showed poor effects of these interventions with no difference compared to placebo according to several outcomes analysed. Therefore, the real benefits of autologous blood and PRP on pain, function, quality of life and patient satisfaction are still debated, and the related costs and risk of injection-related harms such as pain and infection do not seem to justify their use.

Previous systematic reviews also report inconclusive results about the use of PRP and autologous whole blood in this population. A recent systematic review and meta-analysis showed doubts about the superiority of PRP or autologous blood versus corticosteroids⁹ while another study demonstrated mild benefits of these agents when compared with placebo¹⁰. Therefore, autologous whole blood or PRP injection should not be used as the first choice for the treatment of lateral elbow pain.

Among conservative treatments, physical therapy is commonly suggested as the first line of intervention for lateral elbow pain. Physiotherapy usually consists of forearm strengthening exercise, stretching, and hot-cold modalities. In particular, eccentric muscle training seems to be a core treatment of lateral elbow pain, significantly improving arm function, tenderness and strength¹¹. In addition, physical therapy modalities including Extracorporeal Shock Wave Therapy (ESWT) and low-level laser therapy (LLLT) could be associated with therapeutic exercise for pain relief¹². A combination of physiotherapy and physical therapy modalities should be preferred for the treatment of lateral elbow pain, in addition to nonsteroidal anti-inflammatory medications, if needed.

A specific issue in the rehabilitation field is the lack of information about the effectiveness of a combination of these procedures with other rehabilitative interventions for the management of lateral elbow pain. Indeed, only few articles investigating exercise therapy or physical therapy modalities were considered in the review.

In conclusion, data in this review do not support the use of autologous blood or PRP injection for the treatment of lateral elbow pain. Hence it is debatable whether autologous whole blood or platelet-rich plasma injection are promising therapeutic choices for improving pain, function and quality of life of patients with lateral elbow pain. As these approaches do not produce relevant clinical and functional benefits their significant added costs are not justified.

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