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Original article

Inefficacy of ultrasound-guided local injections of autologous conditioned plasma for recent epicondylitis: results of a double-blind placebo-controlled randomized clinical trial with one-year follow-up

Bernard Montalvan[1,2,*], Patrick Le Goux[1,2,*] Shahnaz Klouche[2], Delphine Borgel[3], Philippe Hardy[2,4] and Maxime Breban[1,5]

Abstract

Objectives. The aim was to assess the efficacy of two intra-tendinous injections of platelet-rich plasma (PRP) on epicondylitis of recent evolution ($\leqslant$3 months).

Methods. Our study was a double-blind placebo-controlled randomized trial. Two US-guided injections of either PRP (autologous conditioned plasma) or saline solution were performed with an interval of 4 weeks. The exclusion criterion was previous CS infiltration. Patients were monitored by an independent evaluator blinded to treatment at baseline and 1, 3, 6 and 12 months of follow-up. The primary evaluation criterion was the relative improvement from baseline to 6 months in pain score on visual analog scale (0–10). Secondary criteria were the Roles–Maudsley score and the assessment of pain on isometric contraction of extensor carpi radialis brevis and extensor digitorum communis.

Results. Twenty-five patients were randomly assigned to each group. Three patients in each arm dropped out before 6 months. In both groups, the pain score [mean (S.D.)] decreased significantly between two consecutive visits from 6.8 (0.8) (PRP) and 7 (1) (saline) at baseline to 2.5 (1.6) and 1.6 (1.5) (PRP) and to 2.1 (1.6) and 1.8 (2.1) (saline) at 6 and 12 months, respectively. At 6 months, no statistically significant difference was found between groups for relative improvement in pain score [autologous conditioned plasma: −63.2 (22.4%); saline: −69.7 (25.1%); $P = 0.24$]. No significant difference was found for the secondary criteria.

Conclusion. Two US-guided PRP injections for epicondylitis of recent evolution were not more efficacious than saline injections, until 6- and 12-months follow-up.

Trial Registration: ClinicalTrials.gov; https://clinicaltrials.gov/; NCT02378285.

Key words: lateral humeral epicondylitis, infiltration, platelet-rich plasma, ultrasonography, treatment, randomized control trial.

[1]Hôpitaux Universitaires Paris Ile de France Ouest, AP-HP, Service de rhumatologie, [2]Hôpitaux Universitaires Paris Ile de France Ouest, AP-HP, Service de Chirurgie Orthopédique et Traumatologique, [3]Hôpitaux Universitaires Paris Ile de France Ouest, AP-HP, Service d'Hématologie et d'Immunologie, F-92100 Boulogne-Billancourt, [4]Université de Versailles Saint-Quentin-en-Yvelines, UFR des Sciences de la Santé, Versailles and [5]Université de Versailles Saint-Quentin-en-Yvelines, INSERM U1173, UFR Simone Veil, Laboratoire d'Excellence INFLAMEX, Montigny-le-Bretonneux, France

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Correspondence to: Bernard Montalvan, Hôpital Ambroise Paré, Service de rhumatologie, 9 av Charles de Gaulle, 92100 Boulogne-Billancourt, France. E-mail: bernard.montalvan2@libertysurf.fr

*Bernard Montalvan and Patrick Le Goux contributed equally to this study.

CLINICAL SCIENCE

Rheumatology key messages

- Two US-guided platelet-rich plasma injections for recent epicondylitis were not more efficacious than saline injections.
- Lack of efficacy of platelet-rich plasma injections for recent epicondylitis exists whatever the evaluation criteria and the time point considered.
- Similarly favourable outcomes of US-guided injections were observed in platelet-rich plasma and placebo groups and might have been facilitated by needling.

Introduction

Pain around the lateral epicondyle of the humerus is known by several names, of which the most common is tennis elbow (TE) [1, 2]. TE has an estimated prevalence in the general population of 1.3%, peaks at age 45–54 years, and affects women more frequently than men [3–5]. The estimated annual incidence rate of TE ranges from 4 to 7 per 1000 in the population [6, 7]. TE tends to evolve towards spontaneous resolution with a time frame that varies according to the study from 6 to 24 months [2, 8].

Local injection of glucocorticoid has been used since the 1950s and has for many years been considered a first line of treatment for TE [8]. However, as several studies failed to show a long-term beneficial effect of this procedure [9–13], the search for alternative treatments has intensified. During the past 10 years, therapies have become more focused on the potential use of growth factors as a stimulant of tendon repair. Several studies, mostly performed *in vitro*, have emphasized the restorative properties of platelet-derived factors that have the ability to accelerate the healing of various tissues, such as bone, tendon and muscle. The haemostatic action of platelets consists of aggregation and formation of a procoagulant surface essential for thrombin generation and fibrin formation. Among other proteins, platelets contain in their granules several growth factors, such as PDGF, insulin-like growth factor 1, TGF-β, fibroblast growth factor, VEGF and hepatocyte growth factor [14–16]. Those growth factors are released upon platelet activation and promote tissue remodelling, wound healing and angiogenesis. Based on this knowledge, injections of platelet-rich plasma (PRP), consisting of blood plasma with an enriched concentration of autologous platelets, are frequently used nowadays in the fields of maxillofacial surgery, dentistry and orthopaedics as an adjunctive treatment for situations such as wound or bone healing, alloplastic surgery and muscle/tendon damage repair [15, 16].

Concerning the treatment of TE, a relatively small study comparing the use of PRP *vs* bupivacaine local injection was first reported in 2006 by Mishra and Pavelko [17], showing promising results. More recently, a larger double-blind randomized controlled trial showed that PRP was superior to glucocorticoid injection after 12 months of follow-up [18].

The theory underlying those trials was that intra-tendinous injection of PRP would stimulate repair mechanisms and promote tendon healing [19–21]. In order to address this suggestion further, we decided to test the superiority of injecting PRP for the treatment of recent (⩽3 months) TE in naïve subjects (i.e. who had never been infiltrated for this purpose) *vs* control saline injection. The goal of this treatment procedure was to provide long-term relief of pain, lasting until 6 and/or 12 months of follow-up.

Methods

Study design

This was a single-centre randomized double-blind placebo-controlled study (both patient and evaluator were blinded to the administered treatment). This study was conducted in accordance with the Declaration of Helsinki (1964) and its revision (1975). The patient consent form was approved by the Institutional Review Board of the Ambroise Paré Hospital (Comité de Protection des Personnes Ile-de-France VIII, Boulogne-Billancourt, France), and the subjects' written consent was obtained. The study was approved by the French national security agency for medicine and health products (AFSSAPS, authorization number 2009-A00804-53). The database was declared at the National Commission for Data Protection (Commission Nationale de l'Informatique et des Libertés, CNIL, N°470235). The investigators were two rheumatologists who specialized in sport medicine: P.G. selected the patients for inclusion and performed the TE clinical evaluations, whereas B.M. performed the injections.

Patients

Generalist practitioners, correspondents of our hospital department, were asked to propose the study to their patients who fulfilled the study selection criteria. If the patient was interested in this study, he was referred to the investigator. Fifty volunteer male or female patients, aged between 35 and 65 years, suffering of TE for no more than 3 months and having never received any specific medical or orthopaedic treatment for the current TE, were randomly allocated to receive either active treatment (i.e. PRP injection) or the placebo comparator (i.e. saline injection). Exclusion criteria were as follows: history of TE; previous elbow surgery; diabetes; inflammatory arthritis; anticoagulation; known allergy to local anaesthetics; work accidents; and occupational diseases. The diagnosis of TE was established based on the following validated criteria: pain reproduction upon isometric contraction of extensor carpi radialis brevis (ECRB) and extensor digitorum communis (EDC), while the elbow was being kept in extension; absence of limitation or pain during elbow passive movements; absence of pain during cervical movements; normal neurological examination of the upper limb; and absence of any other source of pain in the elbow, on X-ray. Moreover, evidence for tumoral

involvement had to be ruled out by an US or MRI examination of the elbow.

Treatment procedure

The PRP was prepared using the autologous conditioned plasma device from Arthrex (Naples, FL, USA), following the supplier's instructions. The sampling procedure and injection were performed in compliance with strict aseptic technique. The whole duration of the procedure was 45 min on average. The patient was lying on a table with their arm in the supine position. A nurse collected 12 ml of blood by venipuncture using the double syringe device from Arthrex and placed the needle into the centrifuge. The injector physician (B.M.) discarded the supernatant in order to isolate the platelet concentrate. According to previous reports, the autologous conditioned plasma preparation from Arthrex results in 1.6-fold enrichment of platelets, compared with whole-blood content, without detectable red or white blood cells [22, 23]. The nurse filled a 2 ml syringe with the PRP and another identical syringe with saline solution. The randomization was then performed by the physician; patients randomized to the active treatment group received the PRP, whereas patients from the placebo group received saline, in a blind fashion (the syringe was hidden from the view of the patient). The injector first injected 2 ml of 1% lidocaine s.c. Then he performed the injection of PRP or saline guided by US. For this purpose, the US probe was placed longitudinally, parallel to the common tendon of the lateral epicondyle, to visualize its fibres. The needle, guided by US, was advanced into the tendon, parallel to the tendon fibres, until it achieved bone contact, and then the solution was injected in three or four passages so that the treatment was delivered to superficial, medium and deep tendon sites. If a fissured area was detected on US, as a linear hypo-echoic area or a disruption of fibrillar structure, the injector used the needle to dissect this area. The entire procedure was performed twice for each patient: the first time at inclusion and the second time after an interval of 4 weeks. In the immediate aftermath, the patients were warned that local pain could be exacerbated during the 3–5 days following injection and were recommended to take 1 g of paracetamol and to perform local ice application in the short term. Rehabilitation and physical therapy were neither prescribed nor allowed. Local CS injections were not authorized during the entire study period.

Evaluation

The patients were evaluated for efficacy and safety at 1, 3, 6 and 12 months after inclusion. At each visit, efficacy was assessed using the following clinical variables: the patient's assessment of global pain score on a visual analog scale of 0–10 (primary outcome measure); the Roles–Maudsley score (from 1 to 4); and the triggering of pain on isometric contraction of ECRB and EDC (yes/no answers; secondary outcome measures). At each visit, they were also questioned about potential side effects.

Randomization and blinding

The treatment was allocated according to a randomization list, with a block size of four with no stratification. The evaluator (P.G.) was blinded to treatment because he was not involved in the injection protocol. The patient was also blinded to treatment because the blood sample was collected from all patients and the syringe was hidden after preparation, before randomization.

Statistical analysis

The main criterion was the change of global pain score on visual analog scale between baseline and the 6-month visit. Intragroup and intergroup intention-to-treat analyses were performed using Student's *t*-tests, applying the last-observation carried forward method. Differences of proportions were tested using χ^2. The sample size calculated was 22 patients per group, so that this study had a power of 90% with typel error rate $\alpha = 0.05$ to demonstrate a significantly greater improvement of the global pain score of at least 10% in the PRP over the placebo group with a standard deviation of 0.10. A value of $P < 0.05$ was considered to be statistically significant. We used the SPSS software (version 19 for Windows) to perform statistics.

Results

Study flow chart and patient characteristics

The study was conducted between October 2010 and April 2014; 56 subjects were selected, 3 declined to participate immediately and 3 did not meet the inclusion criteria. Fifty patients were included between 7 October 2010 and 18 April 2013 (25 in each group; Fig. 1). Population characteristics were well balanced between both arms: it consisted of 34 men and 16 women (17 men and 8 women in each group); they had a mean (S.D.) age of 47 (9.2) years in the PRP group and 46.4 (8.6) years in the control group. In the PRP group, 14 of 24 (58%) patients with known information had a manual occupation and/or played tennis or golf, whereas there were 9 of 21 (43%) in the control group. The global pain score at baseline ranged from 5 to 9, and its mean was similar in both groups: 6.8 (0.8) in the PRP and 7 (1) in the control group (Table 1 and Fig. 2A). Baseline secondary criteria were also similar between both groups: the mean Roles–Maudsley score was 3.2 (0.7) and 3.4 (0.5) in the PRP and placebo groups, respectively; all patients in both groups were positive for pain upon isometric contraction of ECRB, whereas 88 and 92% were positive for pain upon contraction of EDC, in the PRP and placebo groups, respectively (Table 1 and Fig. 2B–D).

During the 12-month follow-up period, six patients were lost to follow-up or withdrew from the study because of protocol violation (forbidden CS injection): two after the 1-month visit in the PRP group and one more between the 3- and 6-month visits, one after the 1-month visit in the control group and two more between the 3- and 6-month visits (Fig. 1).

Fig. 1 Study flow chart

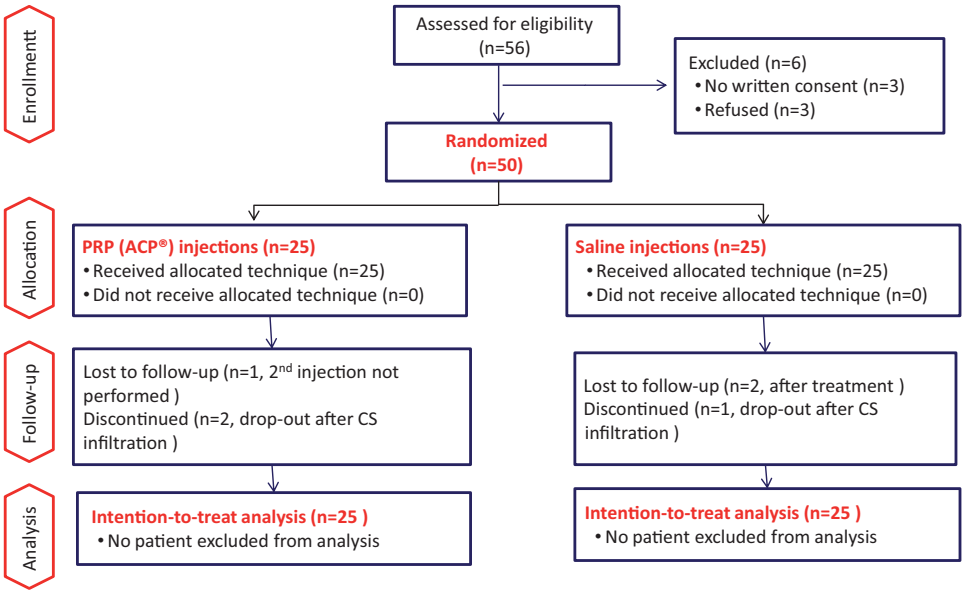


Table 1 Evolution of outcome criteria in tennis elbow patients treated with platelet-rich plasma or saline local injections at inclusion and 1-month visits, until month 12

Outcome measure	M0	M1 (M1–M0)	M3 (M3–M0)	M6 (M6–M0)	M12 (M12–M0)
Global pain score, mean (S.D.)					
PRP	6.8 (0.8)	5.8 (1.9) [−1 (1.7)]	3.6 (1.9) [−3.2 (1.9)]	2.5 (1.6) [−4.3 (1.6)]	1.7 (1.5) [−5.2 (1.3)]
Saline	7 (1)	5.1 (1.6) [−1.9 (1.8)]	3.7 (1.9) [−3.4 (1.9)]	2.1 (1.6) [−4.9 (1.7)]	1.8 (2.1) [−5.4 (2.3)]
Roles–Maudsley score, mean (S.D.)					
PRP	3.3 (0.7)	3.2 (0.6) [−0.1 (0.7)]	3 (0.7) [−0.4 (0.9)]	2.6 (0.8) [−0.7 (1)]	2.3 (1.1) [−1 (1.3)]
Saline	3.4 (0.5)	3.2 (0.5) [−0.2 (0.6)]	2.9 (0.7) [−0.6 (0.7)]	2.5 (0.9) [−0.9 (0.9)]	2.2 (0.9) [−1.3 (0.9)]
Pain on ECRB contraction,[a] % positive					
PRP	100	96 (−4)	92 (−8)	56 (−44)	44 (−66)
Saline	100	100 (−0)	76 (−24)	72 (−28)	52 (−48)
Pain on EDC contraction,[a] % positive					
PRP	88	80 (−8)	68 (−20)	52 (−36)	32 (−56)
Saline	92	88 (−4)	84 (−8)	72 (−20)	56 (−36)

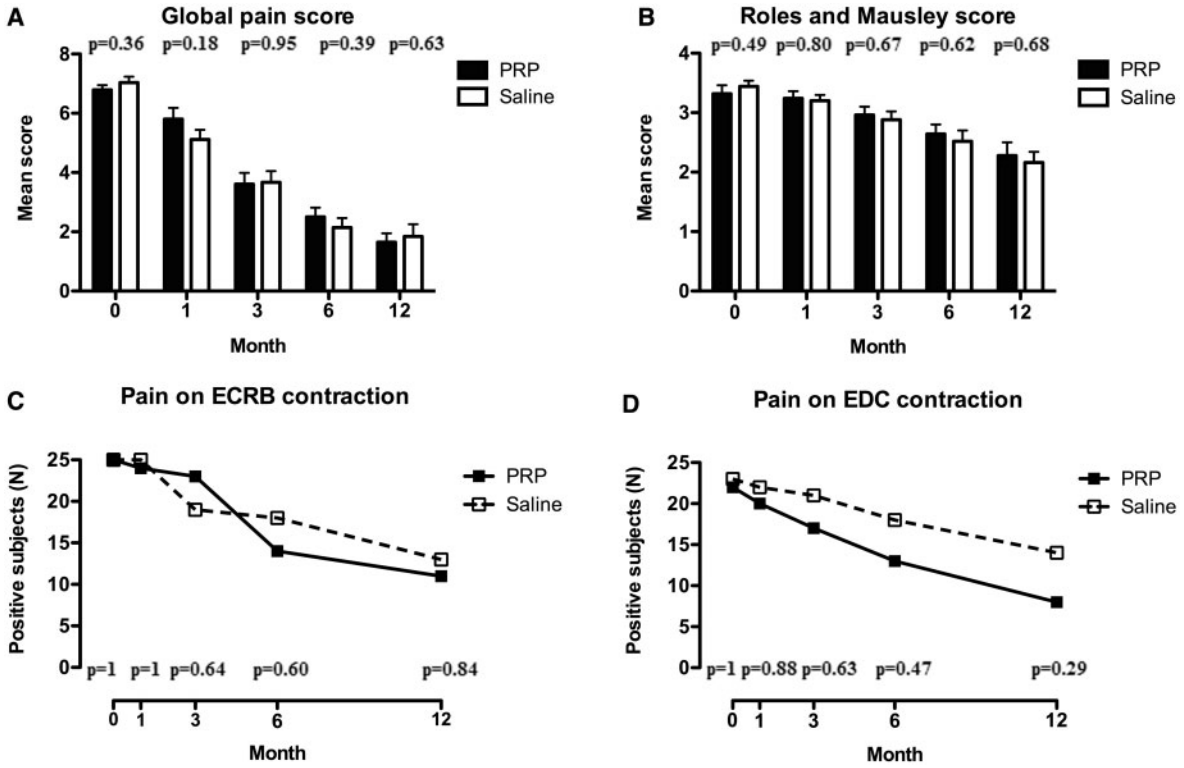
[a]Fifty TE patients in the study (last-observation carried forward analysis). ECRB: extensor carpi radialis brevis; EDC: extensor digitorum communis; M0: month 0; M1: month 1; M3: month 3; M6: month 6; M12: month 12; PRP: platelet-rich plasma.

Efficacy

The evolution of the outcome criteria during entire study is shown in Table 1 and Fig. 2. In each group, the primary outcome criterion (i.e. global pain score) decreased significantly between two consecutive visits throughout the study (intragroup comparison), reaching 2.5 (1.6) and 2.1 (1.6) at 6 months and 1.6 (1.5) and 1.8 (2.1) at 12 months, in the PRP and control groups, respectively. Variations from baseline of the global pain score was not significantly different between groups either at 6 months [PRP: −63.2 (22.4%); control: −69.7 (25.1%); $P = 0.24$] or at any other follow-up time point (intergroup comparison). At 6 months, six patients in the PRP and nine in the control group (i.e. 27 and 41% of the completers, respectively; $P = 0.34$) were considered to be asymptomatic, having reached a pain score $\leqslant 1$. There were 14 (64%) in each group after 1 year.

No statistically significant difference was found for any of the secondary criteria between PRP and control groups: either the functional Roles–Maudsley index evaluation or the pain triggering upon isometric contraction of ECRB and EDC confirmed a favourable evolution of TE

FIG. 2 Evolution of the primary (**A**) and secondary outcome criteria (**B**–**D**) throughout the study



ECRB: extensor carpi radialis brevis; EDC: extensor digitorum communis; PRP: platelet-rich plasma.

during the 12-month period that was comparable between both groups (Table 1). Only the proportion of patients having pain on EDC contraction appeared to decrease more sharply in the PRP than the placebo group, albeit the difference between both arms did not reach statistical significance, even at 1 year (−56% in the PRP *vs* −36% in the saline group; $P = 0.1$).

Safety

Side effects did not occur very often and were relatively mild. The most commonly reported one was pain during and after the injection, which disappeared within 72 h. It affected four (16%) patients in the PRP group and two (8%) in the saline group. In addition, one patient developed a haematoma after saline injection, which disappeared within 3 days, and two other patients reported a local cutaneous allergic reaction after the first injection of PRP. In the latter patients, the second injection was performed without prior local anaesthesia, and chlorhexidine was used instead of iodine solution for disinfection. The allergic phenomenon did not recur. It is noteworthy that no tendon rupture was detected in any group.

Discussion

In this 1-year follow-up randomized controlled trial, two intra-tendinous US-guided injections of PRP were not more effective than two injections of saline for the treatment of TE of recent development (i.e. ⩽3 months duration), whatever the evaluation criteria and the time point considered. Hence, we noted a similar kinetics of decrease in both arms, for all the four evaluation criteria, that reached a low level at the end of the trial.

Several aspects of this study concur to strengthen the validity of its conclusions: the randomization and double-blind design; the homogeneous characteristics of the patients, who were selected by a single physician, had suffered recent epicondylitis and had never been infiltrated; the injection procedure that was guided by US and was performed by a unique operator; and the evaluations that were all performed by the same physician.

Local injections of CSs have remained until now the most widely used method to treat TE. However, several randomized controlled trials failed to show a beneficial effect of such intervention in the long term, that is, beyond 8 weeks, even though short-term improvement was readily demonstrated [10–12]. Moreover, the outcome after 2–12 months of follow-up might be less favourable after CS injections than using conservative therapeutics, such as physiotherapy, NSAID or even no intervention [10–12]. Thus, there is an interest in developing new therapeutic strategies to improve TE evolution, notwithstanding the fact that as many as 84% of the patients included in previous studies had much improved or

completely recovered after 1 year of follow-up, despite the lack of specific intervention (wait-and-see approach) [9, 10]. In this context, the goal of PRP injections is to provide benefit regarding mid- and long-term pain relief, that is, at 6 and 12 months of follow-up, by boosting the healing process.

Early studies of PRP injection for TE showed promising results that were not confirmed by our present work [17, 18]. In a pilot open-label study, Mishra and Pavelko [17] showed statistical evidence for better improvement with PRP containing both concentrated platelets and leucocytes than bupivacaine injection, in a small group of patients suffering from chronic TE (>3 months), despite standard treatment. Another randomized study concluded that PRP was superior to CS injection after 1 year of follow-up [18]. In a more recent large-scale multicentre randomized control trial, Mishra *et al*. [24] confirmed a better outcome after 6 but not after 3 months following PRP, compared with bupivacaine injection. Notably, however, the level of attrition in that study was high at 6 months, which may weaken its conclusions. In contrast to those promising results, several randomized controlled trials comparing PRP with autologous blood injection yielded a negative result after 2–6 months follow-up [25–27]. Variations between the protocols used in different controlled trials, including differences between PRP preparation content and the types of patients recruited, could explain some discrepancies. All PRP preparations are not alike and contain different concentrations of other blood components, as well as different numbers of platelets. The optimal growth factor release, number of platelets and content of associated components for tendon repair have not yet been determined. Notably, one study suggested that an excessively high concentration of platelets may even inhibit tendon healing [28].

In a recent review of all the published randomized clinical trials of PRP injection for TE [29], authors concluded that the single one that could be considered as favourable for PRP was comparing it with CS injections [18]. Moreover, they emphasized that in all those studies but one, which failed to demonstrate PRP superiority [30], the control group was receiving anaesthetic (bupivacaine) or CS injections that might be deleterious, instead of a real placebo. Here, we first performed lidocaine injection outside the tendon and around the peritendon and thereafter PRP or saline injection intra-tendinously. Nevertheless, the possibility cannot be excluded entirely that the presence of lidocaine in the area could have exerted a negative effect on tendon healing.

Moraes *et al*. [31], in a recent Cochrane Collaboration review, compared platelet-rich therapy with placebo, autologous whole-blood injection and dry needling, to assess the effects of platelet-rich therapies for treating musculoskeletal soft tissue injuries. They concluded that the available evidence was insufficient to support the use of PRP for treating those conditions.

Finally, it should be kept in mind that our study concerned only recent TE (⩽3 month of evolution), which had never been infiltrated before, as opposed to other studies that included patients resistant to an initial therapeutic intervention, most often CS infiltration [17, 18]. This may explain the similar favourable outcome observed in both groups in our study, which might have also been facilitated by the US-guided intra-tendinous injections (i.e. needling).

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References

1 De Smedt T, de Jong A, Van Leemput W *et al*. Lateral epicondylitis in tennis: update on aetiology, biomechanics and treatment. Br J Sports Med 2007;41:816–9.

2 Nirschl RP. Elbow tendinosis/tennis elbow. Clin Sports Med 1992;11:851–70.

3 McCormack RR Jr, Inman RD, Wells A *et al*. Prevalence of tendinitis and related disorders of the upper extremity in a manufacturing workforce. J Rheumatol 1990;17:958–64.

4 Ono Y, Nakamura R, Shimaoka M *et al*. Epicondylitis among cooks in nursery schools. Occup Environ Med 1998;55:172–9.

5 Shiri R, Viikari-Juntura E. Lateral and medial epicondylitis: role of occupational factors. Best Pract Res Clin Rheumatol 2011;25:43–57.

6 Verhaar JA. Tennis elbow: anatomical, epidemiological and therapeutic aspects. Int Orthop 1994;18:263–7.

7 Hamilton PG. The prevalence of humeral epicondylitis: a survey in general practice. J R Coll Gen Pract 1986;36:464–5.

8 Murtagh JE. Tennis elbow. Aust Fam Physician 1988;17:90–1, 94–5.

9 Smidt N, Lewis M, Hay EM *et al*. A comparison of two primary care trials on tennis elbow: issues of external validity. Ann Rheum Dis 2005;64:1406–9.

10 Bisset L, Beller E, Jull G *et al*. Mobilization with movement and exercise, corticosteroid injection, or wait and see for tennis elbow: randomized trial. BMJ 2006;333:939.

11 Krogh TP, Bartels EM, Ellingsen T *et al*. Comparative effectiveness of injection therapies in lateral epicondylitis: a systematic review and network meta-analysis of randomized controlled trials. Am J Sports Med 2013;41:1435–46.

12 Lindenhovius A, Henket M, Gilligan BP *et al*. Injection of dexamethasone versus placebo for lateral elbow pain: a prospective, double-blind, randomized clinical trial. J Hand Surg Am 2008;33:909–19.

13 Newcomer KL, Laskowski ER, Idank DM *et al*. Corticosteroid injection in early treatment of lateral epicondylitis. Clin J Sport Med 2001;11:214–22.

14 Roukis TS, Zgonis T, Tieman B. Autologous platelet-rich plasma for wound and osseous healing: a review of the literature and commercially available products. Adv Ther 2006;23:218–37.

15 Ranly DM, McMillan J, Keller T *et al*. Platelet-derived growth factor inhibits demineralized bone matrix-induced intramuscular cartilage and bone formation. J Bone Joint Surg Am 2005;87:2052–64.

16 Molloy T, Wang Y, Murrel GAC. The roles of growth factors in tendon and ligament healing. Sports Med 2003;33:381–94.

17 Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. Am J Sports Med 2006;34:1774–8.

18 Peerbooms JC, Sluimer J, Bruijn DJ *et al*. Positive effect of an autologous platelet concentrate in lateral epicondylitis in a double blind randomized controlled trial: platelet-rich plasma versus corticosteroid injection with a 1-year follow-up. Am J Sports Med 2010;38:255–62.

19 Borzini P, Mazzucco L. Tissue regeneration and in loco administration of platelet derivatives: clinical outcome, heterogeneous products, and heterogeneity of the effector mechanisms. Transfusion 2005;45:1759–67.

20 de Mos M, van der Windt AE, Jahr H *et al*. Can platelet-rich plasma enhance tendon repair? A cell culture study. Am J Sports Med 2008;36:1171–8.

21 Foster TE, Puskas BL, Mandelbaum BR *et al*. Platelet-rich plasma: from basic science to clinical applications. Am J Sports Med 2009;37:2259–72.

22 Bohu Y, Klouche S, Lefevre N *et al*. Efficacité thérapeutique de l'autologous conditioned plasma (ACP): analyse de sa composition cellulaire et revue de la littérature. J de Traumatol du Sport 2013;30:211–5.

23 Mazzoca AD, McCarthy MB, Chowaniec DM *et al*. Platelet-rich plasma differs according to preparation method and human validity. J Bone Joint Surg Am 2012;94:308–16.

24 Mishra AK, Skrepnik NV, Edwards SG *et al*. Efficacy of platelet-rich plasma for chronic tennis elbow: a double-blind, prospective, multicenter, randomized controlled trial of 230 patients. Am J Sports Med 2014;42:463–71.

25 Creaney L, Wallace A, Curtis M *et al*. Growth factor-based therapies provide additional benefit beyond physical therapy in resistant elbow tendinopathy: a prospective, single-blind, randomized trial of autologous blood injections versus platelet-rich plasma injections. Br J Sports Med 2011;45:966–71.

26 Thanasas C, Papadimitriou G, Charalambidis C *et al*. Platelet-rich plasma versus autologous whole blood for the treatment of chronic lateral elbow epicondylitis: a randomized controlled clinical trial. Am J Sports Med 2011;39:2130–4.

27 Raeissadat SA, Sedighipour L, Rayegani SM *et al*. Effect of platelet-rich plasma (PRP) versus autologous whole blood on pain and function improvement in tennis elbow: a randomized clinical trial. Pain Res Treat 2014;2014:191525.

28 Giusti I, Rughetti A, d'Ascenzo S *et al*. Identification of an optimal concentration of platelet gel for promoting angiogenesis in human endothelial cells. Transfusion 2009;49:771–8.

29 De Vos R-L, Windt J, Weir A. Strong evidence against platelet-rich plasma injections for chronic lateral epicondylar tendinopathy: a systematic review. Br J Sports Med 2014;48:952–6.

30 Krogh TP, Fredberg U, Stengaard-Pedersen K *et al*. Treatment of lateral epicondylitis with platelet-rich plasma, glucocorticoid, or saline: a randomized, double-blind, placebo-controlled trial. Am J Sports Med 2013;41:625–35.

31 Moraes VY, Lenza M, Tamaoki MJ *et al*. Platelet-rich therapies for musculoskeletal soft tissue injuries. Cochrane Database Syst Rev 2014;(4):CD010071.