Evaluation of the efficacy of autologous platelet-rich plasma injection versus local corticosteroid injection for the treatment of lateral epicondylitis

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Received 17 August 2017
Accepted 11 September 2017

The Egyptian Orthopaedic Journal
2017, 52:158–164

Background
Local corticosteroid injection is a common treatment procedure for lateral epicondylitis. No statistically important or clinically better results favoring steroid injections were found in recent studies. Platelet-rich plasma (PRP) has shown a broad stimulating effect for repair and is used widely in different sports injuries. This study was performed to evaluate the effectiveness of local injection of autologous PRP versus corticosteroid to treat lateral epicondylitis.
Patients and methods
This prospective, randomized study included 40 patients with lateral epicondylitis: 20 in group A received 2 ml PRP and 20 in group B received 2 ml local corticosteroid. The final results were measured using the visual analog scale (VAS) for pain and Nirschl staging. The follow-up was continued for 6 months, with assessment at the 1st, 4th, 12th weeks and 6th months.
Results
The group B showed a significant pain improvement compared with group A in both VAS and Nirschl stage at the first and fourth weeks follow-up visits. At the 12th week visit, the VAS and Nirschl scores were significantly better in group A. At the sixth month follow-up, group A showed a statistically significant decrease in pain in comparison to group B (VAS P=0.001 and Nirschl P=0.002). At the 6-month final follow-up, nine (45%) patients in group B and 18 (90%) patients in group A were completely relieved of pain (P=0.007).
Conclusion
Autologous PRP is an effective treatment modality compared with corticosteroid injection, with less side effects and recurrence rate.

Keywords:
autologous platelet-rich plasma, elbow, injection, lateral epicondylitis, local corticosteroid

Egypt Orthop J 52:158–164

1110-1148

Introduction

Lateral epicondylitis is a common problem seen in orthopedic practice [1]. Its incidence is about 4–7/1000 yearly in general practice. Its peak incidence is between 35 and 55 years [2]. An epidemiological study reported that 87% involved the dominant arm [3].

Its characteristic clinical picture is tenderness and pain over the lateral epicondyle. It results from cumulative microtrauma due to repetitive wrist extension and alternating forearm supination and pronation. Although the term of tennis elbow is used, it is perceived more in nonathletes than in athletes [4].

The disease pathophysiology is controversial, with not enough scientific evidence in favor of any specific treatment modality [5]. Angiofibroblastic degeneration of the extensor carpi radialis brevis origin and incomplete healing response after repeated microtrauma (tendinosis) was proposed by most current researches [6].

Local corticosteroid injection has used its anti-inflammatory property to treat nonexisting inflammation. One theory to explain the temporary improvement claimed that this results from the bleeding caused by forcing fluid through tissue planes under high pressures [7].

Autologous blood Injection has been tried over the last few years to address the lateral epicondylitis problem and defined to be effective at both intermediate and long-term follow-ups, with major pain improvement [8]. Cellular activity chemical modifiers present in blood and specifically in its platelets are well known to be mitomorphogenic. On the basis of that fact, these growth factors may act as cellular and humoral mediators inducing a healing response [9].

A question was proposed about the use of platelet-rich plasma (PRP) to treat lateral epicondylitis. The objective of this prospective study was to assess the effectiveness and role of autologous PRP injection to treat lateral epicondylitis, compared with the commonly used local corticosteroid injection.

Patients and methods

Patients were between 15 and 70 years of age. Each patient was assessed by history and clinical examination and presented by pain which failed to respond to medical treatment (NSAIDs) and instructions. Patients having one of the following positive clinical tests were included in this study: Elicited tenderness distal and anterior to the lateral epicondyle, pain with resisted wrist extension with full elbow extension, coffee cup test (picking up a full cup of coffee/water associated with localized pain at the region of lateral epicondyle), chair test (picking up a chair with the elbow extended), Thompson test (flexing the patient shoulder to 60° with the elbow extended, forearm pronated and wrist extended 30°, applying pressure to dorsum of the second and third metacarpal in the direction of wrist flexion and ulnar deviation), and Cozen's test (flexing the elbow and extending the wrist against resistance).

Patients with elbow rheumatoid arthritis, dermatomyositis, cervical radiculopathy, suspected infection, malignancy, previous elbow trauma or surgical treatment, local steroid injection within 3 months and those with elbow instability were excluded from this study.

Approval of the local research ethics committee was obtained. The treatment choices were discussed with the patients and consents were taken for this study. Patients were allotted sequentially into two parallel groups: A (autologous PRP group) and B (corticosteroid group), of 20 cases each. Equal randomization (1 : 1 allocation ratio) was undertaken according to a computer-generated randomization table.

Methods

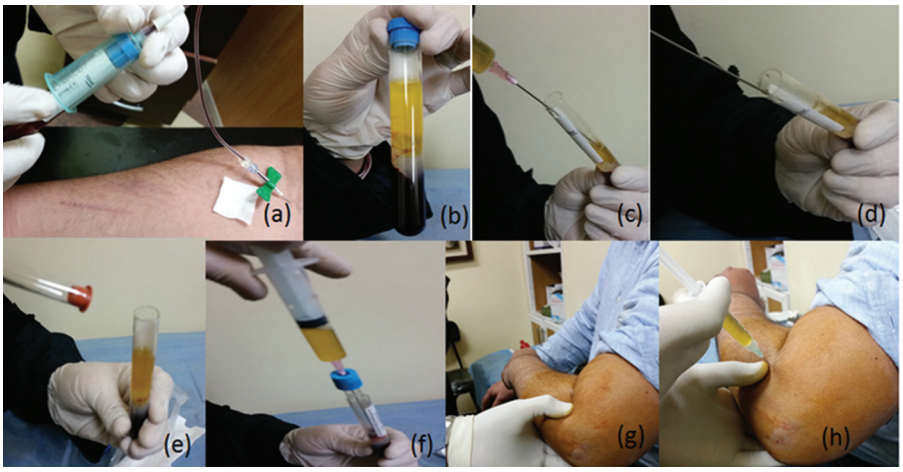
For group A patients, MyCells Autologous Platelet Preparation System was used (Kaylight; ProTech, Orange, California, USA) (Fig. 1). A measure of 10 ml of blood was aspirated in MyCells Vacutainer (Kaylight, Orange, California, USA) with citrate dextrose anticoagulant (Fig. 2a). The tube was shaken gently five times to mix the anticoagulant thoroughly with the blood and it was centrifuged at 3500 rpm for 10 min.

Figure 1

Autologous platelet-rich plasma preparation system.

This yielded around 6–7 ml of plasma present above the gel separator (Fig. 2b). The tube was positioned in the rack and the cap was removed. The upper 4 ml which represents the platelet poor plasma phase was discarded because it contains very low amounts of platelets, growth factors, and proteins (Fig. 2c). The remaining 2–2.5 ml of the plasma above the gel was the PRP phase. To produce the PRP and make full usage of the platelets which form a gluey sedimented layer to the gel surface, the PRP was withdrawn and injected a number of times against the gel (Fig. 2d). The filter provided was then taken and carefully peeled off the wrapping so as not to contaminate the tube (Fig. 2e). Holding the filter with the wrapping, the filter was gradually pushed in with the brown rubber cap end going inside the PRP tube. The gel separator in the PRP tube was gently touched. The long blunt needle provided with the set was then connected to a syringe to extract the PRP in the filter and this constituted the final PRP ready for injection (Fig. 2f). The area to be injected was disinfected with alcohol 70% or betadine. With the patient in supine or sitting posture the elbow was

Figure 2



Technique of autologous platelet-rich plasma (PRP) preparation and injection: (a) blood sampling, (b) the blood after centrifugation showing the plasma above the gel separator, (c) discarding the platelet poor plasma, (d) provisional PRP harvesting, (e) PRP filtration, (f) final PRP harvesting, (g) identification of anatomical bony landmarks, (h) PRP injection.

flexed to 90° with the palm facing down. The anatomical bony landmarks were identified (Fig. 2g). The PRP was injected at the site of maximum tenderness and in the vicinity of the tendon of extensor carpi radialis brevis (Fig. 2h). A small adhesive sterile dressing was applied. The elbow was kept in sling for comfort. Group B patients were designated to receive an injection of local cortiocosteroid. Patients were injected with 2 ml local corticosteroid (methylprednisolone acetate 80 mg) according to the same technique. After 24 h, patients were asked to follow a standardized stretching protocol for 2 weeks. Forearm strengthening exercises were initiated thereafter. At 4 weeks follow-up, patients were allowed to progress with their normal sporting and activities as tolerated.

The outcome measures were visual analog scale (VAS) for pain and the Nirschl staging system [5,10]. The VAS consisted of a 10 cm line marked at one end with 'no pain' and at other end with 'the worst imaginable pain'. The patient was asked to point at where on the line he or she rates the pain (Fig. 3).

The Nirschl staging system consists of seven phases of pain severity in an ascending order (Table 1).

Both VAS and the Nirschl staging system were used to evaluate the patients during the clinic follow-up visits before injection, and at 1, 4, 12 weeks and at the 6 month final follow-up. Complications in both treatment groups were recorded.

The Mann–Whitney *U*-test (nonparametric test) was used to compare the outcome between the two groups in terms of pain. The χ^2-test was used to compare the groups' categorical variables. The *P* values of at least 0.05 are statistically nonsignificant; *P* values less than 0.05 are significant; and *P* values less than 0.01 are highly significant.

Results

Group A consisted of eight male and 12 female patients with a mean age of 44.1 (23–66) years, and group B consisted of seven men and 13 women with a mean age of 41.3 (17–62) years. The groups' characteristics are presented in Table 2.

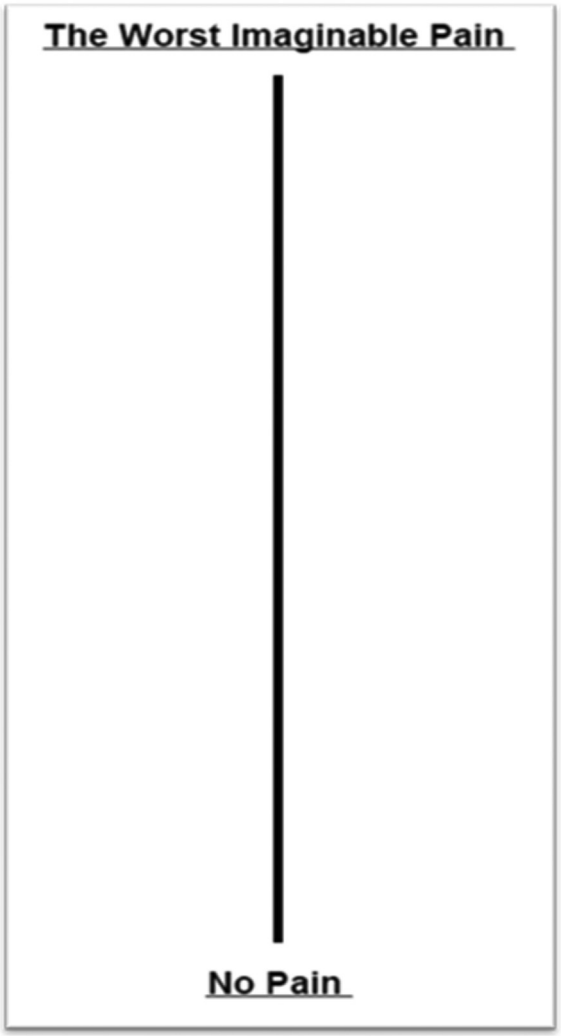
Preinjection, the mean VAS scores for pain were similar in both groups (7.6±0.94 vs. 7.4±0.88, *P*=0.465). Similarly, the mean Nirschl results were 5.2±1.01 vs. 5.1±1.02, *P*=0.735.

At 6 months final follow-up, the pain scores were significantly lower in group A compared with group B (VAS: 0.16±0.48 vs. 1.45±1.43, *P*=0.001; Nirschl grade: 0.1±0.31 *vs.* 0.9±0.91, *P*=0.002) (Tables 3 and 4 and Figs 4 and 5).

The results of both scores followed a quite similar course over the period of follow-up. Early during the follow-up, group A patients reported an unremarkable effect in terms of pain relief with those in group B having significantly lower VAS and Nirschl scores at 1 week. However, at 12 weeks, the VAS and Nirschl scores were significantly lower in group A. This difference was maintained till the final 6-month follow-up. At this final follow-up point, the group B pain scores had begun to rise again compared with the earlier follow-up scores.

At the final 6-month follow-up visit, 18 (90%) patients in group A compared with nine (45%) in group B were completely relieved of pain (P=0.007). However, at the 4-week assessment, 13 (65%) patients in group B had complete relief of pain, and some of them reported recurrences at 6 months, resulting in a rate of recurrence in this group of 30.7% (four of the 13 patients). In comparison, only three (15%) patients in group A were pain free at 4 weeks, but there was a no recurrence by 6 months, and that was statistically significant (P<0.001).

Figure 3



Visual analog scale (VAS).

In group A, 10 (50%) patients complained of an increase in pain immediately (and during the following few days) after the injection, compared with five (25%) in group B but this was statistically insignificant (P=0.191). One (5%) patient in group B had local skin atrophy while none in group A, but this also was not statistically significant (P=1.0), indicating that proper local steroid infiltration avoids or reduces this complication. None of the patients had stiffness of the elbow, infection, neurovascular injury or tendon rupture or other complications in both treatment groups.

Discussion

Lateral elbow pain is a common cause of patients' disability and it is most commonly diagnosed as lateral epicondylitis or tennis elbow. Its peak age incidence is in the fourth decade [2]. There has been much debate about its pathophysiology [11]. Macroscopic or microscopic tears in the origin of the extensor carpi radialis brevis, together with an incomplete healing response is the most widely accepted proposed theory [12,13]. It has been established in histopathological studies that lateral epicondylitis is not of an inflammatory origin; rather, it is an angiofibroblastic degeneration consisting of fibroblastic and vascular response. Thus, it is now more precisely termed tendinosis [14].

Table 1 Nirschl staging system

Phase	Clinical features
Phase 1	Mild pain with exercise, resolves within 24 h
Phase 2	Pain after exercise, exceeds 48 h
Phase 3	Pain with exercise, does not alter activity
Phase 4	Pain with exercise, alters activity
Phase 5	Pain with heavy activities of daily living
Phase 6	Pain with light activities of daily living, intermittent pain at rest
Phase 7	Constant pain at rest, disrupts sleep

Table 2 Characteristics of group A (autologous platelet-rich plasma group) and group B (corticosteroid group)

Characteristics	Group A (n=20)	Group B (n=20)	P-value
Male : female	8 : 12	7 : 13	1.00 (NS)
Age [mean (range)] (years)	44.1 (23–66)	41.3 (17–62)	0.905 (NS)
Side (right : left)	15 : 05	14 : 06	1.00 (NS)
Dominant side [n (%)]	16 (80)	17 (85)	1.00 (NS)
Duration of symptoms [mean (range)] (weeks)	9.3 (2–52)	7.5 (2–34)	0.706 (NS)
Employment [n (%)]			
Manual	9 (45)	6 (30)	0.514 (NS)
Nonmanual	11 (55)	14 (70)	0.514 (NS)

Table 3 Mean visual analog scale for pain for group A (autologous platelet-rich plasma group) and group B (corticosteroid group)

Follow-up	VAS [mean (SD)]		*P*-value
	Group A (autologous PRP) (*n*=20)	Group B (corticosteroid) (*n*=20)	
Preinjection	7.60 (0.94)	7.40 (0.88)	0.465 (NS)
6 months	0.16 (0.48)	1.45 (1.43)	0.001 (HS)

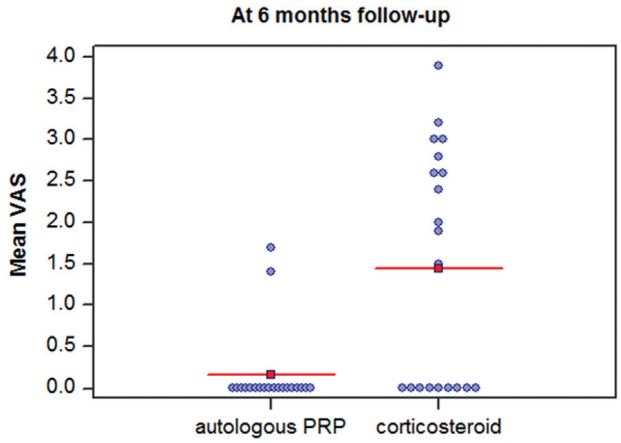
HS, highly significant; PRP, platelet-rich plasma; VAS, visual analog scale.

Table 4 Mean Nirschl staging for group A (autologous platelet-rich plasma group) and group B (corticosteroid group)

Follow-up	Nirschl stage [mean (SD)]		*P*-value
	Group A (autologous PRP) (*n*=20)	Group B (corticosteroid) (*n*=20)	
Preinjection	5.20 (1.01)	5.10 (1.02)	0.735 (NS)
6 months	0.1000 (0.31)	0.90 (0.91)	0.002 (HS)

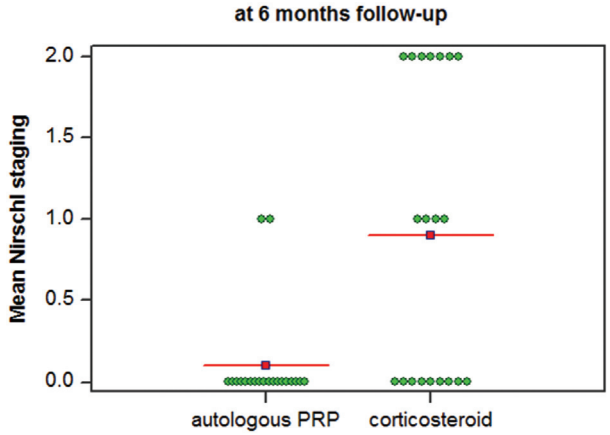
HS, highly significant; PRP, platelet-rich plasma.

Figure 4



Graph showing the mean visual analog scale (VAS) of pain in both groups at 6 months follow-up (the middle line indicating the mean). PRP, platelet-rich plasma.

Figure 5



Graph showing the mean Nirschl staging of pain in both groups at 6 months follow-up (the middle line indicating the mean). PRP, platelet-rich plasma.

It is clear that there is no single effective procedure for all patients as evidenced by the fact that there is more than one type of treatment available. The most commonly used treatment is physical therapy and corticosteroid injections.

In a study by Bisset *et al.* [15], it was concluded that physiotherapy has a more profit to 'watchful waiting' during the first, 6 weeks and to corticosteroid injection after 6 weeks. Extracorporeal shock wave therapy also has lately gained popularity. However, this treatment was shown to be no better than placebo according to a recent, randomized, double-blind study [16].

In their systematic review, Assendelft *et al.* [17] have analyzed the outcome of randomized, controlled studies of corticosteroid injections for lateral epicondylitis. Analysis showed that it is effective on short-term scale only (2–6 weeks) and no difference was found between it and other treatment modalities, including placebo at a follow-up of more than 6 weeks. Moreover, no conclusions could be made about the most useful corticosteroid, its dose, volume, or injection interval [17]. In addition, corticosteroids have a quite high frequency of deterioration and recurrence, probably because of the permanent adverse changes within the structure of the tendon caused by intratendinous injection. In addition, patients tend to misuse the arm as a result of direct pain relief after injection [18]. These results are similar to the results of this study, which showed a minor reversal of the early pain relief in the corticosteroid group by 12 weeks, with high rates of relapse. Animal studies have provided conclusions that intratendinous corticosteroid injections adversely affect the tendon's biomechanical properties [19–22]. The side effects of corticosteroid injection include tendon rupture, sepsis, local skin atrophy, and hyperglycemia [12,22,23].

Using autologous whole blood or PRP for the treatment of different types of tendinosis has gained recent popularity. The concentrated growth factors

within platelets work in synchronization to provoke a healing response in a damaged tendon. This was supported by in-vitro study of Klein *et al.* [24] reported that the transforming growth factor β significantly increases type I collagen production in tendons. Consequently, PRP was hypothesized to regenerate damaged tendons or muscles. The PRP releases its growth factors. These bioactive proteins in turn stimulate local stem cells and enhance extra cellular matrix gene expression [25]. Recruitment of reparative cells from the local circulation or bone marrow then occurs. At the same time, PRP inhibits additional inflammation, apoptosis, and metallo-proteinase activity. These interactive pathways may result in the repair of tendon or muscle tissue, which can bear loading with work or sports activity, thereby decreasing pain. PRP may also modulate the microvascular environment or alter efferent or afferent neural receptors [26].

Edwards and Calandruccio [5], in their study evaluated autologous blood injections in 28 patients with lateral epicondylitis. They found that 22 (79%) patients had pain improvement over 9.5 months follow-up after injection. These patients maintained this profit throughout the path of follow-up evaluation, with no recurrence [5]. Mishra and Pavelko [27] in their study injected PRP for chronic elbow tendinosis. Patients reported 93% pain improvement compared with the preinjection status at the final follow-up.There are few studies in the literature comparing the effectiveness of injection of autologous PRP with injection of local corticosteroid for lateral epicondylitis [28–30]. This study was to assess the efficacy and role of single autologous PRP injection compared with single local corticosteroid injection to treat lateral epicondylitis. In the study, group B showed significant improvements in VAS score and Nirschl stage at 1 and 4 weeks compared with group A. At 6 months after injection, it was found that significantly more patients of group A had complete pain relief in comparison to group B (90 vs. 45%, P=0.007). Despite good early results, with a rate of complete pain relief of 65% at 4 weeks, group B was found more likely to experience repetition of pain, with a rate of 30.7% by final follow-up at 6 months. Bisset *et al.* [15] have described 72% recurrence after 3–6 weeks on longer follow-up.

Conclusion

Autologous PRP injection showed statistically significant lower pain compared with group B at the latest follow-up. This study offers promising results of another treatment that addresses the pathophysiology of resistant lateral epicondylitis. With further studies involving bigger sample size with longer periods of follow-up with possible use of one or more than one injection, a fair conclusion can be drawn with respect to the effectiveness and safety of this treatment modality.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Haahr JP, Andersen JH. Physical and psychosocial risk factors for lateral epicondylitis: a population based case-referent study. Occup Environ Med 2003; 60:322–329.

2 Hamilton PG. The prevalence of humeral epicondylitis: a survey in general practice. J R Coll Gen Pract 1986; 36:464–465.

3 Bernhang AM. The many causes of tennis elbow. N Y State J Med 1979; 79:1363–1366.

4 Teitz CC, Garrett WE, Miniaci A, Lee MH, Mann RA. Instuctional Course Lectures. The American Academy of Orthopaedic Surgeons: tendon problem in athletic individuals. J Bone Joint Surg 1997; 79A:138–152.

5 Edwards SG, Calandruccio JH. Autologous blood injections for refractory lateral epicondylitis. J Hand Surg Am 2003; 28:272–278.

6 Leadbetter WB. Cell-matrix response in tendon injury. Clin Sports Med 1992; 11:533–578.

7 Balasubramaniam P, Prathap K. The effect of injection of hydrocortisone into rabbit calcaneal tendons. J Bone Joint Surg Br 1972; 54:729–734.

8 Connell DA, Ali KE, Ahmad M, Lambert S, Corbett S, Curtis M. Ultrasound guided autologous blood injection for tennis elbow. Skeletal Radiol 2006; 35:371–377.

9 Anitua E, Andía I, Sanchez M, Azofra J, del Mar Zalduendo M, de la Fuente M, *et al.* Autologous preparations rich in growth factors promote proliferation and induce VEGF and HGF production by human tendon cells in culture. J Orthop Res 2005; 23:281–286.

10 Nirschl RP. Elbow tendinosis/tennis elbow. Clin Sports Med 1992; 11:851–870.

11 Boyer MI, Hastings H. Lateral tennis elbow: 'is there any science out there?'. J Shoulder Elbow Surg 1999; 8:481–491.

12 Hay EM, Paterson SM, Lewis M, Hosie G, Croft P. Pragmatic randomised controlled trial of local corticosteroid injection and naproxen for treatment of lateral epicondylitis of elbow in primary care. BMJ 1999; 319:964–968.

13 Nirschl RP. Tennis elbow tendinosis: pathoanatomy, nonsurgical and surgical management. In: Gordon SL, Blair SJ, Fine LJ, editors. Repetitive motion disorders of the upper extremity. Rosemont: American Academy of Orthopaedic Surgeons; 1995. 23. pp. 467–479.

14 Nirschl RP, Pettrone FA. Tennis elbow. The surgical treatment of lateral epicondylitis. J Bone Joint Surg Am 1979; 61A:832–839.

15 Bisset L, Beller E, Jull G, Brooks P, Darnell R, Vicenzino B, *et al.* Mobilisation with movement and exercise, corticosteroid injection, or wait and see for tennis elbow: randomised trial. BMJ 2006; 333:939–948.

16 Haake M, König IR, Decker T, Riedel C, Buch M, Müller HH, *et al.* Extra corporeal shock wave therapy in the treatment of lateral epicondylitis: a randomized multicenter trial. J Bone Joint Surg Am 2002; 84A:1982–1991.

17 Assendelft WJ, Hay EM, Adshead R, Bouter LM. Corticosteroid injections for lateral epicondylitis: a systematic overview. Br J Gen Pract 1996; 46:209–216.

18 Smidt N, van der Windt DA, Assendelft WJ, Devillé WL, Korthals-de Bos IB, Bouter LM. Corticosteroid injections, physiotherapy, or a wait-and-see policy for lateral epicondylitis: A randomised controlled trial. Lancet 2002; 359:657–662.

19 Gottlieb NL, Riskin WG. Complications of local corticosteroid injections. JAMA 1980; 243:1547–1548.

20 Kapetanos G. The effect of the local corticosteroids on the healing and biomechanical properties of the partially injured tendon. Clin Orthop Relat Res 1982; 163:170–179.

21 Unverferth LJ, Olix ML. The effect of local steroid injections on tendon. J Sports Med 1973; 1:31–37.

22 Ketchum LD. Effects of triamcinalone on tendon healing and function: a laboratory study. Plast Reconstr Surg 1971; 47:471–482.

23 Haslock I, MacFarlane D, Speed C. Intra-articular and soft tissue injections: a survey of current practice. Br J Rheumatol 1995; 34:449–452.

24 Klein MB, Yalamanchi N, Pham H, Longaker MT, Chang J. Flexor tendon healing in vitro: effects of TGF-beta on tendon cell collagen production. J Hand Surg Am 2002; 27:615–620.

25 Molloy T, Wang Y, Murrell G. The roles of growth factors in tendon and ligament healing. Sports Med 2003; 33:381–394.

26 Mishra A, Woodall J Jr, Vieira A. Treatment of tendon and muscle using platelet-rich plasma. Clin Sports Med 2009; 28:113–125.

27 Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. Am J Sports Med 2006; 34:1774–1778.

28 Arirachakaran A, Sukthuayat A, Sisayanarane T, Laoratanavoraphong S, Kanchanatawan W, Kongtharvonskul J. Platelet-rich plasma versus autologous blood versus steroid injection in lateral epicondylitis: systematic review and network meta-analysis. J Orthop Traumatol 2016; 17:101–112.

29 Gautam VK, Verma S, Batra S, Bhatnagar N, Arora S. Platelet-rich plasma versus corticosteroid injection for recalcitrant lateral epicondylitis: clinical and ultrasonographic evaluation. J Orthop Surg 2015; 23:1–5.

30 Krogh TP, Fredberg U, Stengaard-Pedersen K, Christensen R, Jensen P, Ellingsen T. Treatment of lateral epicondylitis with platelet-rich plasma, glucocorticoid, or saline: a randomized, double-blind, placebo-controlled trial. Am J Sports Med 2013; 41:625–635.