Comparison of platelet-rich plasma and laser therapy in treatment of chronic lateral epicondylitis

Amr E. Okasha, Amany S. El-Bahnasawy, Ola M. Gharbia, Sherief E. Farrag

Department of Rheumatology and Rehabilitation, Faculty of Medicine, Mansoura University, Mansoura, Egypt

Correspondence to Amany S. El-Bahnasawy, MD, Department of Rheumatology and Rehabilitation, Faculty of Medicine, Mansoura University, Madinet Alsalam, Mansoura, Egypt. Tel: +20 100 241 4718; fax: 0502202878; e-mail: d_amy75@yahoo.com

Received 4 January 2019
Accepted 10 March 2019

Egyptian Rheumatology & Rehabilitation
2019, 46:202–207

Background
Lateral epicondylitis (LE) is the most frequent cause of chronic lateral elbow pain in adults that represents an encumbrance on social and professional life of patients. Many treatment modalities that have been used in the management of LE have recently come into question. Platelet-rich plasma (PRP) and low-level laser therapy (LLLT) have been tried for management of chronic tendinopathies but with some debate about their effectiveness.
Objectives
This study compared the effectiveness of local injection of PRP and LLLT in pain reduction and functional improvement in chronic LE.
Patients and methods
This randomized double-blinded, prospective study included 104 eligible patients with chronic LE. Fifty-two patients were treated with local PRP injection and 52 were treated by intermittent LLLT. They were evaluated at 3 and 6 months for subjective pain using visual analog scale (VAS), functional outcome, and grip strength.
Results
Pain was assessed using the subjective VAS which was improved in both PRP and LLLT groups, DASH score and grip strength revealed improvement in both groups. This improvement was of highly statistical significance in both groups when compared with baseline evaluation ($P<0.001$). On comparing the PRP group with the LLLT group, there was significant improvement in VAS at 6 months only, whereas there were significant improvements in functional outcome and grip strength evaluation at 3- and 6-month follow-up for PRP group.
Conclusion
Treating patients with LE with PRP injection improves pain and function more effectively compared with LLLT.

Keywords:
epicondylitis, laser, platelet-rich plasma

Egypt Rheumatol Rehabil 46:202–207

1110-161X

Introduction

Lateral epicondylitis (LE) is also referred to as tennis elbow. It is the most common overuse syndrome of the elbow in which an injury includes the extensor muscles of the forearm, which originate from the lateral epicondyle of the distal humerus. LE is the most frequent cause of chronic lateral elbow pain in adults [1]. It is a painful condition that influences the origin of common extensor tendon at lateral humeral epicondyle followed by lack of function, so it represents a burden on social and professional life of patients [2]. The overall prevalence rate of LE ranges from 1 to 3% of population yearly [3]. Chronic LE with duration of symptoms more than 3 months is a degenerative process that occurs as a result of repetitive microtrauma in activities that require strong hand grip and forceful wrist movement. Individuals at high risk are those with aged between 25 and 50 years [4,5].

Many treatment modalities have been used in the management of LE, including bracing, rest, NSAIDs, physiotherapy, extracorporeal shockwave therapy, and acupuncture [6]. Moreover, local corticosteroid or whole autologous blood injection and various surgical procedures have been advocated. Many of these treatments have recently come into question [7]. Platelet-rich plasma (PRP) represents new therapeutic option for chronic tendinopathies that is used to enhance tissue regeneration with the advantages of easy preparation, low cost, minimally invasive administration, in addition to high safety [8]. Low-level laser therapy (LLLT) also represents one of the physical modalities that have been tried for treatment of LE with conflicting results [9,10].

Aim of the study

The aim of this study was to compare the effectiveness of local injection of autologous PRP and LLLT in reducing pain and improving function in patients with chronic LE of elbow.

Patients and methods

Study design

This is a randomized double-blinded trial, prospective interventional study. The protocol for this study was approved by the Institutional Research Board of Faculty of Medicine, Mansoura University, with code number R/17.06.136. Patients were randomly selected by closed envelope, and all of them gave written informed consents after having been given detailed information about the content and form of the study.

Patients

This study was conducted from August 2015 to February 2017; patients were recruited from the rheumatology outpatient clinic at Physical Medicine, Rehabilitation and Rheumatology department, in Mansoura University Hospital. A total of 104 eligible patients with chronic LE were assigned randomly to one of the two treatment groups. Group 1 (n=52) was treated with local PRP injection (PRP group), and group 2 (n=52) was treated by intermittent LLLT for 12 sessions (laser group). The inclusion criteria were age within range from 18 to 70 years, presence of pain on the outer aspect of the elbow lasting more than 3 months, and tenderness with direct palpation on lateral humeral epicondyle and with resisted wrist dorsiflexion [11]. All patients have tried primary conservative treatment in the form of physiotherapy and NSAIDs.

The following patients were excluded: those with systemic diseases (such as diabetes mellitus and hypothyroidism); patients with rheumatoid arthritis or other active inflammatory disease of elbow; patients with concurrent carpal tunnel syndrome, ipsilateral shoulder, or cervical spine pain owing to different causes; patients with disorders of coagulation, infective pathology, or neoplastic lesion; patients with history of previous surgical interference or steroid injection for LE within past 3 months; those with history of trauma around elbow and unstable elbow (evaluated by varus–valgus instability test); and finally, pregnant patients and patients using contraceptive drugs [12,13].

All patients were subjected to assessment of medical and rheumatologic history and thorough clinical general and rheumatologic examination. Visual analog scale (VAS) is used for assessment of pain, in which total score ranges from 0 (no pain) to 10 (worst possible pain) [14]. Disability of arm, shoulder, and hand (DASH) score was used to measure functional outcome; total score ranges from 0 (no disability) to 100 (severest disability) [15]. Grip strength was tested unilaterally on the affected hand using hand dynamometer [16].

Preparation and application of platelet-rich plasma

Overall, 60 ml of blood was taken from every patient and divided between six 10-ml tubes that contained anticoagulant (sodium citrate). These tubes were centrifuged immediately using DMO 412 clinical centrifuge (Dragon Laboratory Instruments Limited, Beijing, China). Two spins of centrifugation were done; the first spin was at 1800 rpm for 15 min to separate white blood cells and erythrocytes from other components of blood, whereas second spin was at 3500 rpm for 10 min for further concentration of platelets [17]. The platelet count was done before and after preparation. At least two times increase in platelet concentration makes PRP agreeable [18]. Asepsis and antisepsis procedures were performed using chlorhexidine [6]. Patients were given local field block in the form of 1 ml of 2% xylocaine [17]. Then we used a 22-G syringe to inject PRP into the common extensor tendon. Injection was given by peppering technique [19]. After 24 h, patients started standardized stretching exercises for 2 weeks followed by strengthening forearm exercise. Normal sporting and recreational activities were allowed as tolerated after 3 weeks following injection [20].

Laser therapy technique

LLL therapy is done using Endolaser 422, Enraf-Nonius apparatus (Enraf, Rotterdam, Netherlands). We used 904-nm wavelength lasers. Laser probe is applied perpendicular to skin at point of maximal tenderness around lateral epicondyle. Duration of each session is 5 min for 12 sessions [20]. Forearm strengthening program was initiated as in the PRP injection technique.

All patients were evaluated at baseline and on regular follow-up visits at 1, 3, and 6 months after treatment.

Sample size calculation

A previous study reported that DASH score after 6 weeks was significantly better in the PRP group than in the individual control group (34.1±21.6 and 31.2 ±20.8, respectively) [21]. Considering level of significance of 5%, and power of study of 80%, the sample size calculated for this study is 52 patients in each group.

Table 1 Comparison of age, disease duration, dominance, and adverse effects

			Student's *t*-test	
	PRP	LLLT	*t*	*P*
Age (mean±SD) (years)	38.8±9.9	36.9±9.9	0.981	0.329
Sex [*n* (%)]				
Females	27 (51.9)	28 (54.9)	0.092	0.762
Males	25 (48.1)	23 (45.1)		
Duration of symptoms (months)	6.4±2.2	6.1±2.2	0.790	0.431
Dominant hand right [*n* (%)]	46 (88.5)	47 (92.2)	0.401	0.527
Affected side right [*n* (%)]	41 (78.8)	36 (70.6)	0.930	0.335

LLLT, low-level laser therapy; PRP, platelet-rich plasma.

Table 2 Comparison of the visual analog scale between the platelet-rich plasma and low-level laser therapy groups at the baseline and through the follow-up

			Student's *t*-test	
	PRP (mean±SD)	LLLT (mean±SD)	*t*	*P*
At baseline	8.0±0.7	7.9±0.8	0.927	0.356
1-Month follow-up	6.3±0.7	6.0±0.8	1.853	0.067
3-Month follow-up	2.7±0.7	2.8±0.8	1.853	0.067
6-Month follow-up	1.4±0.8	1.8±0.6	2.638	0.010
ANOVA test				
F	860.527	466.384	–	–
P	<0.001	<0.001	–	–

ANOVA, analysis of variance; LLLT, low-level laser therapy; PRP, platelet-rich plasma.

Statistical analysis

The data collected were coded, processed, and analyzed using SPSS program (version 20) for windows. All data were tested for normality of distribution. Continuous data were exhibited as mean±SD if they were normally sectioned and displayed as median and interquartile range if abnormally distributed. The categorical data were displayed as number and percentage.

Comparisons of data were done using Student's *t*-test, analysis of variance test, Mann–Whitney *U*-test, or χ^2-test as appropriate. In all tests, *P* values less than 0.05 were rated to be statistically significant.

Results

The study comprised 104 patients with LE treated in the period from August 2015 till February 2017. Overall, 103 patients of them (55 females and 48 males) completed 6-month follow-up: 52 in the PRP group and 51 in the LLLT group. Patients of both PRP group and LLLT group were comparable regarding mean age, sex distribution, hand dominance, and mean duration of symptoms (Table 1).

Pain was assessed using the subjective VAS, which was improved in both PRP and LLLT groups ($P<0.001$ for both). There were no significant differences between both groups after 1- and 3-month follow-up; however, at 6-month follow-up, pain improvement was significantly better in PRP injection group ($P=0.010$; Table 2).

Functional outcome evaluation with DASH score revealed improvement in both groups. This improvement was highly significant in both groups when compared with baseline evaluation ($P<0.001$). Moreover, there was statistically considerable improvement in PRP group compared with LLLT at 3- and 6-month follow-up ($P<0.001$ for both; Table 3).

Grip strength evaluation showed similar pattern of improvement. This improvement was highly significant in both groups when compared with baseline evaluation ($P<0.001$), whereas there were significant improvements in grip strength in the PRP group compared with the LLLT group at 3- and 6-month follow-up ($P=0.37$ and <0.001, respectively; Table 4). No adverse effects were reported in any of the patients in both groups (Fig. 1).

Discussion

LE is one of the most frequent causes of musculoskeletal pain involving the common extensor origin from the lateral humeral epicondyle. This disorder results from repetitive overexertion of wrist

Table 3 Comparison of the disability of arm, shoulder, and hand between the platelet-rich plasma and low-level laser therapy groups at the baseline and through the follow-up

			Student's *t*-test	
	PRP (mean±SD)	LLLT (mean±SD)	*t*	*P*
At baseline	86.2±6.0	84.5±7.9	1.255	0.212
1-Month follow-up	74.9±7.0	72.9±7.1	1.428	0.156
3-Month follow-up	41.9±9.6	47.6±7.2	3.429	<0.001
6-Month follow-up	23.7±11.2	37.9±7.9	7.395	<0.001
ANOVA test				
F	573.257	324.761	–	–
P	<0.001	<0.001	–	–

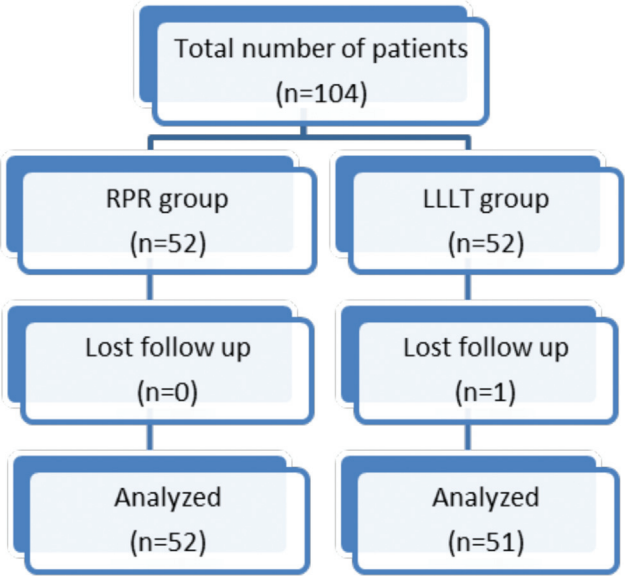
ANOVA, analysis of variance; LLLT, low-level laser therapy; PRP, platelet-rich plasma.

Table 4 Comparison of the grip strength between the platelet-rich plasma and low-level laser therapy groups at the baseline and through the follow-up

			Student's *t*-test	
	PRP (mean±SD)	LLLT (mean±SD)	*t*	*P*
At baseline	17.3±2.2	16.6±2.4	1.589	0.115
1-Month follow-up	20.9±2.1	20.±1.9	2.037	0.044
3-Month follow-up	24.4±2.4	23.9±2.0	2.115	0.037
6-Month follow-up	26.4±2.2	24.9±1.7	3.861	<0.001
ANOVA test				
F	166.975	149.231	–	–
P	<0.001	<0.001	–	–

ANOVA, analysis of variance; LLLT, low-level laser therapy; PRP, platelet-rich plasma.

Figure 1



Flowchart of the study. LLLT, low-level laser therapy; PRP, platelet-rich plasma.

and fingers extensor muscles and leads to significant affection of quality-of-daily-life activities [22]. The availability of multiple treatment options points out that no single procedure is suitable for all patients. Physiotherapy and corticosteroid injections are the most common recommended treatments [17]. Physiotherapy for the treatment of LE comprised physical modalities like LLLT, extracorporeal shockwave therapy, current stimulation or pulsed electromagnetic fields, and also movement therapies [23]. The recurrence of pain is frequent after corticosteroids injection. This may be explained by recurrent hand overuse by patients after pain relief after injection and also by adverse changes that may occur in the tendon structure after steroid injection [24]. There is a conflict in result in trials studying the effect of LLLT in treatment of LE. Earlier studies of laser therapy showed no-effect results, whereas more recent studies showed some improvement in patients receiving laser therapy versus placebo therapy [25]. Different mechanisms have been suggested to explain the biostimulatory effect of LLLT on tissues like reduction of TNF alpha levels [26] and reduction of cell apoptosis [27], although there are no clear data about precise method by which this occurs.

PRP is ever more being used in the treatment of persistent nonhealing tendon injuries including the elbow, patella, and the Achilles. Studies suggest that PRP can influence inflammation and facilitate soft tissue healing process [28] as platelets contain plenty of essential growth factors and cytokines [29]. It has been proposed that PRP improves tissue healing by different mechanisms like enhancement of cellular chemotaxis, cellular proliferation, and differentiation. Moreover, it may promote angiogenesis, lay down extracellular matrix, and help in the removal of

tissue debris, so affects tendon healing capability [30]. The concentrated growth factors in PRP were found to increase production of type I collagen in tendon sheath fibroblasts [31]. At the same time, PRP inhibits excess inflammation, apoptosis, and metalloproteinase enzyme activity [32]. PRP may also alter efferent or afferent neural receptors [17]. These interactive pathways may result in enhancement of initial tendon healing process, restoration of tendon or muscle tissue, and improvement of pain [32].

Our results are comparable to those described by Mishra and Pavelko [19] who noticed significant symptom improvement in VAS after 2 and 6 months. Our results are also in agreement with Tonk *et al.* [20] who compared treatment of LE with LLLT versus PRP, but they assessed pain only and concluded that the LLLT is better in short-term period, whereas PRP was better in pain improvement over long range of follow-up. Both Creaney *et al.* [33] and Thanasas *et al.* [34] reported encouraging results for PRP in their studies comparing PRP and autologous blood injection in patients with LE. Lam and Cheing [35] assessed short-term outcome of laser therapy compared with placebo and reported significant improvement at 3 weeks ($P<0.0125$). Positive results of laser therapy were also obtained with Stergioulas [36] and Emanet *et al.* [37] who reported significant difference ($P<0.05$) regarding improved pain and grip strength.On the contrary, our results were not in agreement with those done by Lundeberg *et al.* [38] who reported no difference between laser and placebo groups up to 3 months after treatment. In addition, Haker and Lundeberg [39] studied the effect of laser applied to acupuncture points and observed no significant disparity between the laser group and placebo group after 10 treatments or at the follow-ups. Moreover, Krasheninnikoff *et al.* [38] compared LLLT versus placebo for patients with LE and found no significant difference between both groups 10 weeks after the last treatment; however, they did not involve 25% of subjects lost to follow-up. In addition, there were another two randomized, double-blind, controlled studies on patients with LE [40,41] that did not elucidate a significant variance in results between laser therapy and placebo. The difference in results may be attributed to different doses of laser therapy.

Conclusion

Treatment of patients with LE with PRP injection improves pain and function more effectively compared with LLLT. The limitations of this study include lack of radiologic evaluation and inability to estimate different growth factor concentrations existing in the PRP. However, further studies that comprise a larger sample size and longer follow-up periods are recommended.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1 Bowen RE, Dorey FJ, Shapiro MS. Efficacy of nonoperative treatment of lateral epicondylitis. Am J Orthop 2001; 30:642–646.

2 Silverstein B, Welp E, Nelson N. Claims incidence of work-related disorders of the upper extremities. Am J Public Health 1995; 88:1827–1833.

3 Buchbinder R, Green S, Struijs P. Musculoskeletal disorders: tennis elbow. Clin Evid 2008; 05:1117–1137.

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

5 Ogden JA, Alvarez RG, Levitt R, Marlow M. Shock wave therapy (Orthotripsy) in musculoskeletal disorders. Clin Orthop Relat Res 2001; 387:22–40.

6 Palacio EP, Schiavetti RR, Kanematsu M, Ikeda TM, Mizobuchi RR, Galbiatti JA. Effects of platelet-rich plasma on lateral epicondylitis of the elbow: prospective randomized controlled trial. Rev Bras Ortop 2016; 51:90–95.

7 Karaduman M, Okkaoglu MC, Sesen H, Taskesen A, Ozdemir M, Altay M. Platelet-rich plasma versus open surgical release in chronic tennis elbow: a retrospective comparative study. J Orthop 2016; 13:10–14.

8 Kaux JF, Crielaard JM. Platelet-rich plasma application in the management of chronic tendinopathies Acta Orthop Belg 2013; 79:10–15.

9 Bjordal JM, Couppe C, Ljunggren AE. Low level laser therapy for tendinopathy: evidence of a dose response. Phys Ther Rev 2001; 6:91–99.

10 Vasseljen OJr, Høeg N, Kjeldstad B, Johnsson A, Larsen S. Low level laser versus placebo in the treatment of tennis elbow. Scand J Rehabil Med 1992; 24:37–42.

11 Regan W, Grondin P, Morrey BF. Lateral epicondylitis (tennis elbow). In: DeLee J, Drez D, Miller M, editors. DeLee and Drez's orthopaedic, sports medicine. 3rd ed. Philadelphia, PA: Saunders Elsevier 2009. 1197–1204

12 Huskisson EC. Measurement of pain. Lancet 1974; 2:1127–1131.

13 Smidt N, Assendelft WJ, van der Windt DA, Hay EM, Buohbinder R, Bouter LM. Cortioosteroid injections for lateral epicondylitis: a systematic review. Pain 2002; 96:23–40.

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

15 Beaton DE, Katz JN, Fossel AH, Wright JG, Tarasuk V, Bombardier C. Measuring the whole or the parts? Validity, reliability, and responsiveness of the Disabilities of the Arm, Shoulder and Hand outcome measure in different regions of the upper extremity. J Hand Ther 2001; 14:128–146.

16 Rompe JD, Decking J, Schoelnner C, Theis C. Repetitive low-energy shock wave treatment for chronic lateral epicondylitis in tennis players. Am J Sports Med 2004; 32:734–743.

17 Vijaya BT, Hardikar SM, Lande O. Autologous platelet rich plasma therapy in Lateral Epicondylitis of Elbow. J Trauma Orthop Surg 2015; 10:3–6.

18 Gosens T, Peerbooms JC, van Laar W, den Oudsten BL. Ongoing positive effect of platelet-rich plasma versus corticosteroid injection in lateral epicondylitis: a double-blind randomized controlled trial with 2-year follow-up. Am J Sports Med 2011; 39:1200–1208.

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

20 Tong G, Kumar A, Gupta A. Platelet rich plasma versus laser therapy in lateral epicondylitis of elbow. Indian J Orthop 2014; 48:390–393.

21 Slichter SJ. Controversies in platelet transfusion therapy. Annu Rev Med 1980; 31:509–540.

22 Yadav R, Kothari SY, Borah D. Comparison of local injection of platelet rich plasma and corticosteroids in the treatment of lateral epicondylitis of humerus. J Clin Diagn Res 2015; 7:5–7.

23 Weber C, Thai V, Neuheuser K, Groover K, Christ O. Efficacy of physical therapy for the treatment of lateral epicondylitis: a meta-analysis. BMC Musculoskelet Disord 2015; 16:223.

24 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.

25 Sims SE, Miller K, Elfar JC, Hammert WC. Non-surgical treatment of lateral epicondylitis: a systematic review of randomized controlled trials. Hand (N Y) 2014; 9:419–446.

26 Aimbire F, Albertini R, Pacheco MT, Castro-Faria-Neto HC, Leonardo PS, Iversen VV, *et al.* Low-level laser therapy induces dose-dependent reduction of TNFalpha levels in acute inflammation. Photomed Laser Surg 2006; 24:33–37.

27 Carnevalli CM, Soares CP, Zângaro RA, Pinheiro AL, Silva NS. Laser light prevents apoptosis in Cho K-1 cell line. J Clin Laser Med Surg 2003; 21:193–196.

28 Antitua E, Andia I, Sanchez M, Azofra J, Del Mar Zalduendo M, Fuente M. Autologous preparations rich in growth factors promote proliferation and induce VEGF and HGF productions by human tendon cells in culture. J Orthop Res 2005; 25:281–286.

29 Ferrari M, Zia S, Valbonesi M. A new technique for hemodilution, preparation of autologous platelet-rich plasma and intraoperative blood salvage in cardiac surgery. Int J Artif Organs 1987; 10:47–50.

30 Sanchez AR, Sheridan PJ, Kupp LI. Is platelet-rich plasma the perfect enhancement factor? A current review. Int J Oral Maxillofac Implants 2003; 18:93–103.

31 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.

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

33 Creaney L, Wallace A, Curtis M, Connell D. Growth factor based therapies provide additional benefit beyond physical therapy in resistant elbow tendinopathy: a prospective, double blind, randomized trial of autologous blood injections versus platelet rich plasma injections. Br J Sports Med 2011; 45:966–971.

34 Thanasas C, Papadimitriou G, Charalambidis C, Paraskevopoulos I, Papanikolaou A. 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; 39:2130–2134.

35 Lam LK, Cheing GL. Effects of 904-nmlow-level laser therapy in the management of lateral epicondylitis: a randomized controlled trial. Photomed Laser Surg 2007; 25:65–71.

36 Stergioulas A. Effects of low-level laser and plyometric exercises in the treatment of lateral epicondylitis. Photomed Laser Surg 2007; 25:205–213.

37 Emanet SK, Altan LI, Yurtkuran M. Investigation of the effect of Ga As laser therapy on lateral epicondylitis. Photomed Laser Surg 2010; 28:397–403.

38 Krasheninnikoff M, Ellitsgaard N, Rogvi-Hansen B, Zeuthen A, Harder K, Larsen R, Gaardbo H. No effect of low power laser in lateral epicondylitis. Scand J Rheumatol 1994; 23:260–263.

39 Haker E, Lundeberg T. Laser treatment applied to acupuncture points in lateral humeral epicondylalgia. A double-blind study. Pain 1990; 43:243–247.

40 Papadopoulos ES, Smith RW, Cawley M, Mani R. Low-level laser therapy does not aid the management of tennis elbow. Clin Rehabil 1996; 10:9–11.

41 Basford JR, Sheffield CG, Cieslak KR. Laser therapy: a randomized, controlled trial of the effects of low intensity Nd : YAG laser irradiation on lateral epicondylitis. Arch Phys Med Rehabil 2000; 81:1504–1510.