

Non-surgical treatment of lateral epicondylitis: a systematic review of randomized controlled trials

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Abstract

Background Non-surgical approaches to treatment of lateral epicondylitis are numerous. The aim of this systematic review is to examine randomized, controlled trials of these treatments.

Methods Numerous databases were systematically searched from earliest records to February 2013. Search terms included “lateral epicondylitis,” “lateral elbow pain,” “tennis elbow,” “lateral epicondylalgia,” and “elbow tendinopathy” combined with “randomized controlled trial.” Two reviewers examined the literature for eligibility via article abstract and full text.

Results Fifty-eight articles met eligibility criteria: (1) a target population of patients with symptoms of lateral epicondylitis; (2) evaluation of treatment of lateral epicondylitis with the following non-surgical techniques: corticosteroid injection, injection technique, iontophoresis, botulinum toxin A injection, prolotherapy, platelet-rich plasma or autologous blood injection, bracing, physical therapy, shockwave therapy, or laser therapy; and (3) a randomized controlled trial design. Lateral epicondylitis is a condition that is usually self-limited. There may be a short-term pain relief advantage found with the application of corticosteroids, but no demonstrable long-term pain relief. Injection of botulinum toxin A and prolotherapy are superior to placebo but not to corticosteroids, and botulinum toxin A is likely to produce concomitant extensor weakness. Platelet-rich plasma or autologous blood injections have been found to be both more and less effective

than corticosteroid injections. Non-invasive treatment methods such as bracing, physical therapy, and extracorporeal shockwave therapy do not appear to provide definitive benefit regarding pain relief. Some studies of low-level laser therapy show superiority to placebo whereas others do not.

Conclusions There are multiple randomized controlled trials for non-surgical management of lateral epicondylitis, but the existing literature does not provide conclusive evidence that there is one preferred method of non-surgical treatment for this condition. Lateral epicondylitis is a condition that is usually self-limited, resolving over a 12- to 18-month period without treatment.

Level of Evidence Therapeutic Level II. See Instructions to Authors for a complete description of level of evidence.

Keywords Elbow tendinopathy · Extensor tendinopathy · Lateral elbow pain · Lateral epicondylalgia · Lateral epicondylitis · Tennis elbow

Introduction

Lateral epicondylitis is a common source of lateral elbow pain. Population studies have shown a prevalence of 1.3 % among those between 30 and 64 years of age, peaking between 45 and 54. It typically affects the dominant upper extremity and is associated with repetitive and forceful activity [53]. Pain is often most pronounced with wrist extension.

Lateral epicondylitis is believed to be a degenerative process, which stems from repetitive microtrauma. Typically, samples from the affected tissue demonstrate angiofibroblastic hyperplasia at the extensor origin of the forearm [60]. Activities requiring repeated contraction of the wrist extensors are implicated, with the extensor carpi radialis brevis (ECRB) tendon most commonly involved. Studies comparing cadaveric and surgical specimens indicate that lateral epicondylitis

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evolves through several stages, beginning with degenerative angiogenesis and ending with fibrosis and calcification [38, 49, 60].

The majority of patients diagnosed with lateral epicondylitis can be effectively managed without surgery, as it is usually a self-limited process from which up to 90 % of patients will recover by 1 year without surgical intervention [5, 12, 60]. Non-surgical approaches to treatment are numerous. The aim of this review is to examine randomized controlled trials (RCTs) of the non-surgical treatment of lateral epicondylitis.

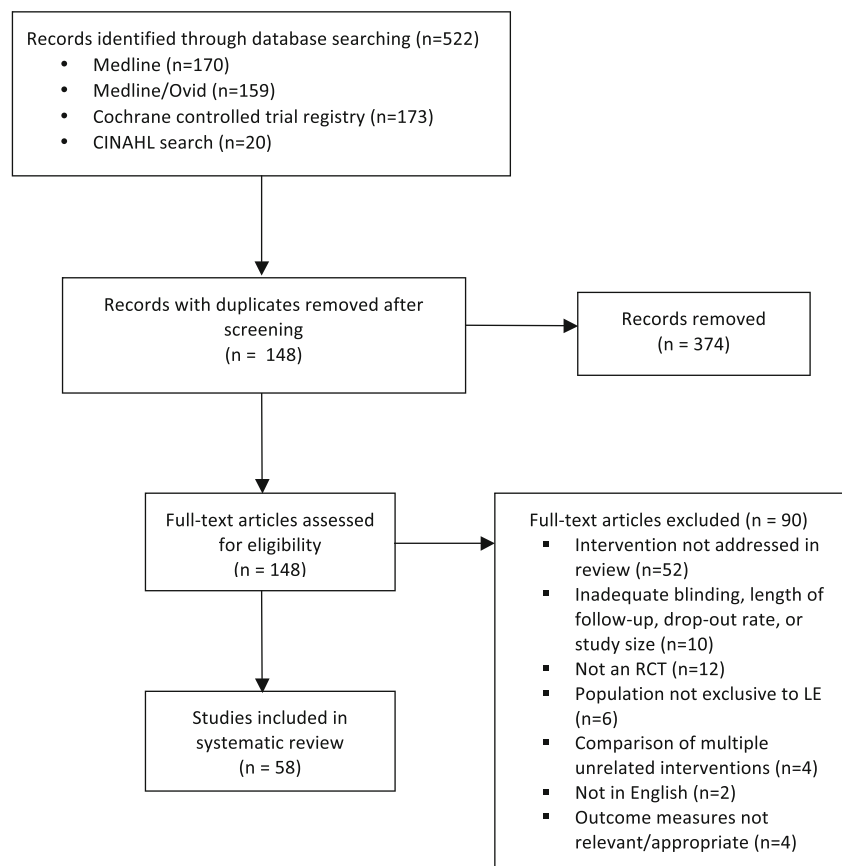
Materials and Methods

Study Identification

Articles from Medline/Ovid, Cochrane Database of Systematic Reviews, and CINAHL were systematically searched from earliest records to February 2013 (Fig. 1). Search terms included “lateral epicondylitis,” “lateral elbow pain,” “tennis elbow,” “lateral epicondylalgia,” and “elbow tendinopathy” combined with “randomized controlled trial.” The abstracts of the resulting articles were

reviewed by two of the authors for the following eligibility criteria: (1) a target population of patients with symptoms of lateral epicondylitis; (2) evaluation of treatment of lateral epicondylitis with one of the following non-operative techniques: corticosteroid injection, injection technique, iontophoresis, botulinum toxin A injection, prolotherapy, platelet-rich plasma (PRP) or autologous blood (ABI) injection, bracing, physical therapy (PT), shockwave therapy, or laser therapy; and (3) a RCT design. Articles meeting the above criteria based on the abstract were considered for inclusion, and full text was retrieved. The quality of each article was assessed according to randomization, blinding, outcome measures, and proportion of patients lost to follow-up. Only articles representing level I or II evidence for a particular intervention were included. This represents double-blind RCTs or single-blind studies for interventions in which blinding was either impossible or had little potential effect on outcome measures. Loss to follow-up was limited to 20 %, with few exceptions, which are noted in the text. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed wherever applicable. A summary of all articles included in this review can be found in Table 1.

Fig. 1 Flow diagram representing process of study identification. *RCT* randomized controlled trial, *LE* lateral epicondylitis



Results

Corticosteroid Injection

Injection of corticosteroid into the area over the origin of the ECRB or point of maximal tenderness has been a common treatment for relief of lateral elbow pain. Dexamethasone, betamethasone, and triamcinolone have been variously used mixed with a local anesthetic such as lidocaine or bupivacaine.

A study by Hay et al. [23] examined the management of lateral epicondylitis with corticosteroid injection, naproxen, or placebo tablets. At 4 weeks, injection showed clear advantage with 92 % of patients in this group reporting they were completely pain free or improved. Only 57 % of the naproxen group and 50 % of the placebo group reported the same. At 12 months, however, no differences were found between the groups.

Corticosteroid injection, physical therapy, and a wait-and-see approach were compared by Verhaar et al. [66] using a scoring system based on subjective pain relief, patient satisfaction, grip strength, and provoked pain to rate outcomes for treatment with corticosteroid injection or physical therapy. At 6 weeks, patients receiving corticosteroid injection had significantly ($p < 0.05$) more excellent and good results than the physical therapy group. There was no difference when the groups were compared at 1 year; however, at that point, 50 % of the patients had had other therapy or surgery. Another short-term study comparing corticosteroid injection, physical therapy, both injection and therapy, and no treatment was performed by Tonks et al. [62]. This study had similar results at 7 weeks, with the injection only group performing significantly ($p < 0.045$) better than other treatment groups. However, 23 % of participants were lost to follow-up in this study.

Smidt et al. [54] assessed long-term outcomes in a RCT comparing corticosteroid injection, physical therapy, and wait-and-see. Corticosteroid injections were found to be the most effective treatment at 6 weeks but were surpassed by physical therapy and no treatment by 52 weeks. Results from later studies by Bisset et al. [6, 7] found comparable results using the same treatment groups. Physical therapy and corticosteroid injection were more effective than wait-and-see before 6 weeks. At 52 weeks, however, there was no difference between physical therapy and wait-and-see, and subjects receiving an injection fared worse than those in other treatment groups. A recent study by Coombes et al. [11] found similar short-term improvement with corticosteroid injections over placebo at 4 weeks; however, these patients fared worse at 26 and 52 weeks of follow-up.

Two double-blind RCTs compared the effects of corticosteroid combined with local anesthetic injection to an injection of local anesthetic alone. Newcomer et al. [37] randomized patients to receive betamethasone/bupivacaine or bupivacaine

alone. All patients also received physical therapy. The only statistically significant ($p < 0.04$) finding was a better visual analog scale (VAS) pain score in the corticosteroid group between 2 and 6 months. Lindenhovius et al. [31] compared injection of dexamethasone and lidocaine with lidocaine alone. No difference was found in any outcome measure at 1- or 6-month follow-ups.

Injection Technique

The peppering technique was described almost 50 years ago [48] and involves many small injections delivered by inserting a needle, injecting, withdrawing without exiting the skin, repositioning, and injecting again until the sensation of crepitus felt with these injections disappears. This technique is thought to initiate healing of the tendon by creating new channels through degenerative tissue in which bleeding occurs [3].

Altay et al. [3] compared injection of corticosteroid plus local anesthetic to local anesthetic alone using the above technique. A second injection of the same type was given at a 2-week follow-up in patients whose symptoms persisted. Results were categorized as excellent, good, fair, or poor according to modified Verhaar criteria (pain relief, patient satisfaction, grip strength, presence of provoked pain on resisted wrist extension). No difference between the two groups was found up to 1 year post-injection, concluding that injection technique is more important than the substance injected.

Dogramaci et al. [16] randomized patients to receive either a single injection of corticosteroid plus local anesthetic, a peppered injection of corticosteroid plus local anesthetic, or a peppered injection of local anesthetic alone. Patients receiving peppered injection of corticosteroid plus local anesthetic had significant ($p < 0.011$) improvement in VAS and a higher percentage of excellent results according to the Verhaar criteria than the other groups at 6 months. Okcu et al. [41] found similar results when they compared single and peppered injections of corticosteroid, assessing the outcome with Disabilities of the Arm, Shoulder, and Hand (DASH) scores (Turkish). Statistically significant ($p < 0.017$) results in favor of the peppered injection group were found at 1 year, but results of this study did not include the 38 % of patients with inadequate follow-up.

Iontophoresis

Iontophoresis involves the use of a small electric current to drive charged molecules through the skin, allowing topical medications to penetrate deeper tissues. Demirtas and Oner [15] studied the short-term effects of iontophoresis of two well-known non-steroidal anti-inflammatory drugs (NSAIDs), sodium diclofenac and sodium salicylate.

Table 1 Characteristics of included studies

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Hay, 1999	164 patients with new episode of LE	(1) Injection of 20 mg methylprednisolone plus lignocaine methylprednisolone provided by UpJohn and naproxen by Syntex (2) Naproxen 500 mg twice daily for 2 weeks	Patient and doctors aware of treatment but assessor was blinded	Primary: participant global assessment of improvement (5-point scale) Secondary: pain, function, and main complaint on Likert scale	4 weeks, 6 months, 12 months; patients not restricted from receiving additional intervention	1/164	At 4 weeks, 92 % of injection group, 57 % naproxen group, and 50 % placebo group were completely better or improved; the difference between injection and other groups was statistically significant. Results at 12 months not statistically significant	Injection: local skin atrophy at the lateral epicondyle (3); naproxen: GI side effects (4), allergic reaction, edema (1)	Funded by Arthritis Research Campaign;
(3) Placebo tablets									
Verhaar, 1996	106 patients with LE not previously treated with Cyriax physiotherapy	(1) Injection of 1 mL, 1 % triamcinolone with 1 mL, 1 % lidocaine +/- 2nd and 3rd injections at 2 and 4 weeks; injections given at extensor origin (2) Cyriax physiotherapy, 12 treatments over 4 weeks	Patient blinding not possible, no mention of assessor blinding	Primary: Verhaar criteria Secondary: grip strength	6 weeks, 52 weeks; patients not restricted from receiving additional interventions after 6 weeks	3/106 patients not assessed at 6 weeks	At 6 weeks, 69 % success rate in injection group vs 27 % of physiotherapy group, this difference was statistically significant. No difference between groups at 52 weeks	None	No benefits received from a commercial party related directly or indirectly to subject of this article
Tonks, 2007	48 patients with LE not treated in prior 6 months	(1) Single injection 10 mg triamcinolone plus 2 % lignocaine (2) Physiotherapy (3) Injection plus physiotherapy (4) No treatment; injections given at point of maximum tenderness	Patient blinding not possible, no mention of assessor blinding	Primary: pain free grip strength Secondary: extensor strength, PRFEQ, complications of treatment	7 weeks	11/48; 41 % dropout rate from physiotherapy groups	Patients receiving injection statistically significantly better for all outcome measures, no significant effect of physiotherapy for any outcome measure, no significant interaction found between physiotherapy and injection	Injection: skin depigmentation and atrophy and injection site (1)	None reported
Smidt, 2002	185 patients with LE for at least 6 weeks, no physiotherapy or injections in	(1) Injection of 10 mg triamcinolone with 1 mL, 2 % lidocaine +/- 2nd and 3rd injection	Patient blinding not possible, research	physiotherapist doing assessment blinded	Primary: general improvement 6-point Likert scale; severity of main complaint, pain during the	3, 6, 12, 26, and 52 weeks	2/178	At 6 weeks, injection group significantly better in all outcome measures (92 % success vs 47 % for physiotherapy and	Injection: facial flush (2), skin irritation (3), red swollen elbow (2), skin color

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
	prior 6 months				day, and inconvenience on 11-point scale, modified pain-free function questionnaire (PFFQ), researcher assessed overall severity			32 % for wait-and-see). At 52 weeks, injection group significantly worse than other intervention groups but no significant difference between physiotherapy and wait-and-see	change over elbow (7)
		No conflict of interest; funded by Health Insurance Council and Netherlands Organization for Scientific Research		(2) 9 physiotherapy treatments over 6 weeks	Secondary: PFG, MGS, pain-pressure threshold				Physiotherapy: skin irritation (3), red swollen elbow (3), skin color change over elbow (3)
(3) Wait-and-see									
Bisset, 2006	198 patients with LE for at least 6 weeks, no treatment for 6 months	(1) Injection of 10 mg triamcinolone and 1 mL, 1 % lidocaine +/- 2nd injection at 2 weeks (2) 8 physiotherapy treatments over 6 weeks (3) Wait-and-see	Patient blinding not possible, assessor and study personnel blinded	Primary: global improvement on 6-point Likert scale (completely recovered or much improved considered success), pain-free grip force, assessor's rating of severity, recurrence rates beyond 6 weeks Secondary: VAS, PFFQ	3, 6, 12, 26, and 52 weeks	8/198	At 6 weeks, injection group had significantly better outcomes with 78 % success vs 27 % for wait-and-see and 65 % for physiotherapy. Injection group had significantly more recurrences than other treatment groups. At 52 weeks, physiotherapy had significantly better outcomes than injection but no significant difference in any primary outcome compared to wait-and-see	Injection: loss of skin pigment (2), atrophy of subcutaneous tissue (1)	Funded by University of Queensland and the National Health and Medical Research Council, Primary Health Care Project Grant
Bisset, 2007	Patient data extracted from 2 RCTs: Bisset (2006) and Smidt (2002) outlined above	Treatment groups of respective studies; analysis of the following subgroups performed: baseline pain on VAS (<60, >60), duration of symptoms (<14 weeks,	See individual studies	Global improvement on 6-point Likert scale	Patient data from 6- to 52-week follow-up used	See individual studies	Subgroups of patients determined by baseline patient characteristics do have significantly different outcomes over time	See individual studies	See individual studies

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Coombes, 2013	165 patients with unilateral LE for at least 6 weeks	>14 weeks), previous history of symptoms, employment status (manual, non-manual, no work) (1) CSI of 10 mg/mL of triamcinolone acetone in a 1 mL injection plus 1 mL of 1 % lignocaine (2) Placebo injection 0.5 mL of 0.9 % isotonic saline (3) CSI and 8 weekly PT sessions (4) Placebo and 8 weekly PT sessions	Assessors blinded, patients were blinded to injection type but not to PT	6-point Likert scale, VAS, PRTEE, EuroQol EQ-5D, use of non-allocated treatments, adverse events	4, 8, 12, 26, and 52 weeks	2/165 patients lost to follow-up	4 weeks: Treatment with CSI or PT alone showed improvement with lower complete recovery or improvement, no difference in groups with or without physical therapy 26; 52 weeks: CSI subcutaneous atrophy, hand numbness, vomiting, swelling, skin irritation	Pain after CSI/PT, transient depigmentation or subcutaneous atrophy, hand numbness, vomiting, swelling, skin irritation	2 authors received payment for lectures and a book chapter
Newcomer, 2001	39 patients with LE for less than 4 weeks and no prior treatment	(1) Injection of 6 mg betamethasone and 4 mL, 0.25 % bupivacaine (2) Injection of 5 mL, 0.25 % bupivacaine; patients not allowed to undergo any other prescribed treatment during 6-month study period	Subjects and physician performing injections were blinded to medication used	VAS, functional pain questionnaire, MGS	4 and 8 weeks, telephone follow-up at 6 months (excluding grip strength)	4/39 discontinued to pursue alternative treatment	Both groups improved in a statistically significant manner over time, there were no significant differences in outcome between groups with the exception of an improvement in VAS in the injection group from 8 weeks to 6 months	None reported	None reported
Lindenhovius, 2008	64 patients with LE for less than 6 months, no prior treatment with CSI or iontophoresis	(1) Injection of 4 mg dexamethasone and 1 mL, 1 % lidocaine (2) Injection of 2 mL, 1 % lidocaine; patients free to pursue other forms of treatment during study	Patient and treating surgeon blinded to treatment	DASH, VAS, MGS	1 and 6 months	6 patients dropped from study, 6 patients missed 1-month follow-up, 9 patients missed 6-month follow-up; included in analysis until dropout	Both groups improved over time, no statistically significant difference between groups in any outcome measure at 1 or 6 months	Slight discoloration of skin around injection site (2 placebo, 1 dexamethasone)	None reported
Altay, 2002	120 patients with LE, no prior CSI	(1) Injection of 2 mL lidocaine (2) Injection of 1 mL lidocaine and 1 mL triamcinolone; peppering technique	Patient and assessor blinded to injection type	Verhaar criteria	2, 6, and 12 months	0/120	Both groups improved over time, no statistically significant difference between groups at 2 months, results	No complications observed	None reported

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Dogramaci, 2009	75 patients with LE, no prior CSI	used for both groups, option for 2nd injection at 2 weeks (1) Injection of 1 mL triamcinolone and 1 mL lidocaine (2) Peppered injection of 1 mL lidocaine (3) Peppered injection of 1 mL triamcinolone and 1 mL lidocaine; all groups +/- 2nd injection at 3 weeks	Patient and assessor blinded to injection type	VAS, Verhaar criteria (excellent or good outcomes considered successful)	3 weeks and 6 months	Not discussed	No statistically significant differences between groups at 3 weeks; at 6 months, successful outcomes statistically higher and VAS statistically lower in peppered CS injection group than other treatment groups	No complications observed	None reported
Okcu, 2012	80 patients with LE, no prior CSI	(1) Injection of 1 mL betamethasone and 1 mL prilocaine (2) Peppered injection of 1 mL betamethasone and 1 mL prilocaine; injections given at point of maximum tenderness	Patient could not be blinded to peppering, assessor blinded to injection technique	Turkish DASH	3, 6, 12, 18 months, and final follow-up (average 21.6 months)	31/80, not included in analysis	A statistically significant difference in favor of the peppered injection group was found for DASH scores at 12 and 18 months and at final follow-up	None reported	Authors declare no conflict of interest
Iontophoresis									
Demirtas, 1998	40 patients with LE	(1) Dermal iontophoresis of sodium diclofenac followed by infrared treatment (2) Dermal iontophoresis of sodium salicylate followed by infrared treatment	Not discussed	Pain with pressure to LE, with resisted wrist extension, during functional activity, and at rest	18 days	None	Statistically significant improvement in both groups	None	None reported
Labelle, 1997	129 patients with LE, no steroid intake in prior 6 weeks, no NSAID use in prior 3 weeks	(1) Long-arm cast immobilization and daily slow release diclofenac 150 mg (2) Long-arm cast immobilization and daily placebo; cast was removed at 14 days, medication given daily for 28 days; no other medication for LE allowed during study period	Patients and assessor blinded to treatment	Primary: MPFGS Secondary: MPFGS ratio of affected to normal side, MGS, MGS ratio, VAS (pain and function), pain-free function index	14, 21, and 28 days	1/129	At 28 days, all outcomes improved for both groups in a statistically significant manner. The difference between groups was only statistically significant for VAS (pain) and MGS ratio, in favor of the NSAID group	Headache (4 placebo, 2 NSAID), abdominal pain (6 placebo, 19 NSAID), diarrhea (13 placebo, 25 NSAID)	Supported by grant from National Health and Welfare Canada, Ciba-Geigy Canada provided both NSAID and placebo

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Nirschl, 2003	199 patients with medial or lateral epicondylitis for less than 3 months, no CSI in prior year	(1) Dermal iontophoresis of dexamethasone (2) Dermal iontophoresis of sodium chloride; 6 treatments within 15 days; patients were not to begin other treatments until after 2 day follow-up	Patients and investigator blinded to treatment	Primary: investigator's global evaluation of improvement (-1, worsened, to 4, no symptoms), patient's global evaluation of improvement on same scale, VAS Secondary: patient's assessment of symptoms (0, none, to 4, very severe), investigator's tenderness evaluation on same scale Primary: grip strength, PRTEE	2 days (in person) and 1 month (by phone) post-treatment	9/199	Dexamethasone produced a statistically significant improvement in VAS (23 vs 14 mm for placebo) and more scores of moderate or better on the investigator's global improvement scale (52 vs 33 % at 2 days post-treatment, but outcomes were not significantly different between groups at 1 month	Dexamethasone: application site vesicles (2), blister (2), localized skin reaction (2), burning sensation (1), atopic dermatitis (1), erythema (1), hypersensitivity (1), pruritus (1), skin irritation (1) Placebo: pruritus (3), erythema (2), arthralgia (2), application site pain (1), application site pruritus (1), burning sensation (1), elbow pain (1)	Supported by a grant from Iomed, Inc, Salt Lake City, Utah, who also provided solution
Stefanou, 2012	101 patients with LE less than 2 years, no steroid medication within 6 months	(1) Self-contained iontophoresis patch in place for 2 days with 10 mg dexamethasone in reservoir, +/- second patch replaced 2–10 days after removal of first (2) Injection of 10 mg dexamethasone (3) Injection of 10 mg triamcinolone; treatment for all groups included an 8-week protocol of rest, mobility, and strengthening	Patients could not be blinded to treatment, physician who determined work status not blinded to treatment	Primary: grip strength, PRTEE Secondary: work status (no restrictions, work with restrictions, no work	Completion of 8-week protocol, 6 months after completion of 8-week protocol	19/101 left the study due to non-compliance, treatment failure, or loss to follow-up and were excluded from analysis	Iontophoresis group had statistically significant increase in grip strength at both follow-ups while the other 2 groups only achieved this by 6 months; all 3 groups had statistically significant improvement in PRTEE (pain and function) at 6-month follow-up; improvement in work status at the first follow-up was only statistically significant for the iontophoresis group	Injection; post-injection pain (<10 % patients) Iontophoresis: skin irritation (1)	None reported
Botulinum toxin Hayton, 2005	40 patients with LE for more		Patient, physician administering	MGS, VAS, QOL measured with	3 months	2 patients had an operation (1	At 3 months, there were no significant	Transient extensor lag (12/18 patients	Authors did not receive benefits

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Wong, 2005	60 patients with LE for more than 3 months; no prior injection	(1) Injection of 50 U of botulinum toxin type A in 2 mL normal saline (2) Injection of 2 mL normal saline; injections administered 5 cm distal to area of maximal tenderness in line with the middle of the wrist	(1) Injection of 60 U of Dysport botulinum toxin	Patient and physician blinded to injection type	Primary: VAS	4 and 12 weeks	No loss to follow-up	At 4 weeks, the botulinum group showed a statistically significant improvement in VAS over the placebo group, which was maintained at 12 weeks; no significant difference in grip strength was found between groups at any time	Botulinum: post-injection pain (2), weakness in finger extension (10), paresis of digits (4)
(2) Injection of an equivalent volume of normal saline; injections administered 1 cm from the lateral epicondyle and were aimed toward the tender spot	Secondary: MGS	Funded by a donation from New World Development Ltd. Sponsor had no part in design of study, data collection or interpretation, or final manuscript preparation	Placebo: post-injection pain (1), post-injection nausea (1), weakness in finger extension (6)						
Placzek, 2007	132 patients with LE for more than 4 months, 3 or more conservative	(1) Injection of 60 U botulinum toxin A in 0.6 mL normal saline (2) Injection of 0.6 mL normal saline; injections administered 3–4 cm	Patient and assessor blinded to injection type	Clinical pain score, VAS (continuous pain past 48 h, max pain past 48 h), MGS, global	2, 6, 12, and 18 weeks	2/132	Improvement was more statistically significant for the botulinum group than the placebo group in the clinical pain score	Strength of extension of the third finger was decreased significantly in the botulinum group at 2 weeks, this	1 or more authors received outside funding or grants in excess of \$10,000 from Ipsen Pharma in

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Espandar, 2010	therapies tried without success	distal to tender epicondyle (1) Injection of 60 U botulinum toxin A in 1 mL of normal saline a previous course of PT and/or CSI	Patient and physician blinded to injection type	assessment of improvement by patient and physician (4, substantially better, to 0, substantially worse)	4, 8, and 16 weeks	No loss to follow-up	at every follow-up and in VAS for continuous pain and global assessments of improvement from the 6th week onward	weakness resolved by week 18	support of their research for or preparation of this work
Lin, 2010	16 patients (19 elbows), no CSI in prior 3 months	(1) Injection of 50 U botulinum toxin type A in 1 mL normal saline (2) Injection of 1 mL, 40 mg triamcinolone; injections into the ECRB muscle near common extensor origin	Patient, and assessor blinded to injection type	VAS pain, pain-free grip strength, WHO QOL-BREF questionnaire to assess quality of life	4, 8, and 12 weeks	1 patient did not receive post-treatment evaluations, excluded from analysis	At 4 weeks, both groups reported decreased pain with a significantly greater reduction reported by the steroid group, this pain remained reduced at 8 and 12 weeks but difference between groups were not significant. No statistically significant differences in QOL were observed between groups at any time	All patients in botulinum toxin A group experienced mild weakness in wrist and middle digit extension that resolved by 12 weeks	Study funded by Council of Labor Affairs of Taiwan government. Allergan Inc. provided Botox. Authors report no conflict of interest

Prolotherapy

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Scarpone, 2008	24 patients with LE for at least 6 months and failure of conservative treatments, no CSI in prior 6 weeks	(1) 0.5 mL prolotherapy injections (50 % dextrose, 5 % sodium morhuate, 4 % lidocaine, 0.5 % sensorcaine) (2) Injections of 0.5 mL normal saline; 3 injections administered into supracondylar ridge, lateral epicondyle, and annular ligament for total of 1.5 mL at baseline, 4, and 8 weeks	Patient and physician blinded to injection type	Primary: resting elbow pain on 11-point Likert scale Secondary: resting grip strength, isometric resistance strength	8 and 16 weeks, telephone interview at 52 weeks	4/24 patients dropped out of study, excluded from analysis	The prolotherapy group, but not the control group, showed a statistically significant improvement in pain scores at 8 and 16 weeks. Isometric strength for the prolotherapy group improved significantly at 8 and 16 weeks, the difference between groups were statistically significant at 16 weeks	Prolotherapy: local erythema, irritation, and discomfort 1 day after injection (2), all patients experienced self-limited post-injection pain	Authors have no financial interest in the products mentioned in this article
Carayannopoulos, 2001	24 patients with LE from 3 months to 2 years, no CSI in prior 6 months	(1) Injection of 1 mL procaine, 0.9 mL of P2G (phenol 1.2 %, glycerine 12.5 %, dextrose 12.5 % in sterile water), and 0.1 mL sodium morhuate (2) Injection of 1 mL procaine and 1 mL methylprednisolone; above solutions split between 3 injection sites: annular ligament, origin of common extensor tendon, radial collateral ligament at tubercle of radius; repeat injections at 1 month	Patient and physician blinded to injection type	Primary: VAS Secondary: quadruple VAS (QVAS), DASH, grip strength, pain free grip strength	1 and 3 months, telephone follow-up at 6 months	7/24, lost to follow-up, excluded from analysis	The prolotherapy group experienced a statistically significant improvement in VAS, QVAS, and DASH at 3 and 6 months, while the steroid group only saw this improvement in QVAS at 6 months and in DASH at 3 and 6 months. No significant differences between groups were observed at any time	1 patient from prolotherapy group withdrew from study because of excessive pain, no other adverse reaction reported by patients	Peer reviewers and all others who control content have no relevant financial relationships to disclose
Zeisig, 2008	32 patients (36 elbows) with LE for more than 3 months, no interventions in prior 3 months	(1) Injection of 0.5 mL polidocanol (2) Injection of 0.5 mL lidocaine plus	Patient and physician blinded to injection type	Primary: patient satisfaction with treatment (yes/no), VAS (elbow pain during grip activities of daily life) Secondary: MGS	3 months; patients in group 2 offered injection of polidocanol after initial 3-month follow-up, all patients followed up	2/36 withdrew from trial before first follow-up, not included in analysis	There were no statistically significant differences between treatment groups for any outcome measures at any time. Patients in both groups had	Patients in group 2 noted increased elbow pain and stiffness during first week after injection, no other adverse effects	Authors declare no conflict of interest

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Peerbooms, 2010	100 patients with LE for more than 6 months, failed conservative therapy	epinephrine; injections delivered to target vessels inside extensor origin under ultrasound guidance (1) PRP injection (PRP collected with Recover system by Biomet Biologes) (2) Injection of triamcinolone 40 mg/mL with epinephrine; for both groups 1 mL was injected directly into area of maximum tenderness, remaining solution was injected into common extensor tendon using peppering technique; use of NSAIDs prohibited	Patient and assessor blinded to injection type	VAS, DASH; successful treatment defined as more than 25 % reduction in VAS or DASH without a reintervention at 1 year	12 months after 1st injection 4, 8, 12, 26, and 52 weeks	8/100 lost to follow-up, included in analysis with last data point carried forward	statistically significant decreases in VAS at both follow-ups Success rates were 49 and 73 % according to VAS and 51 and 73 % according to DASH for the steroid group and PRP group respectively. These differences were statistically significant in favor of the PRP group	Apart from local inflammation causing increased pain 3–4 weeks after PRP injection, no systemic or other local reactions were seen	Sponsored by Biomet, the funding source had no involvement in study design; collection, analysis, and interpretation of data; writing of report; or decision to submit for publication
Grosens, 2011	Continuation of Peerbooms (2010)	According to Peerbooms (2010)	Patient and assessor blinded to injection type	VAS, DASH; successful treatment defined as more than 25 % reduction in VAS or DASH without a reintervention at 2 years	2 years	8/100 lost to follow-up, included in analysis with last data point carried forward	Differences in success rates according to VAS and DASH were statistically significant in favor of the PRP group Compared with baseline VAS and DASH scores, a number of patients deteriorated at 2 years, with more patients being from the steroid group. This difference was statistically significant for both VAS and DASH scores	Apart from local inflammation causing increased pain 3–4 weeks after PRP injection, no systemic or other local reactions were seen	Biomet supplied the Recover system used at a discounted rate but did not have any influence on the collection and analysis of data
Kazemi, 2010	60 patients with a new episode of LE; no CSI in prior 3 months	(1) Injection of AB with 2 % lidocaine (2) Injection of 20 mg methylprednisolone	Patients not blinded because blood taken for ABI but assessors	Primary: VAS (within last 24 h) Secondary: pain-free function	4 and 8 weeks	No loss to follow-up	Differences in outcome measures between groups was statistically significant in favor of	There were no noticeable or reported side effects of treatment in either group	Authors report no conflict of interest

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Krogh, 2013	60 patients with LE for at least 3 months, tendinopathy on US	with 2 % lidocaine; injections given proximal to lateral epicondyle; no other therapy allowed for duration of study (1) Injection of 3–3.5 mL PRP (prepared with Biomet GPS II); injections delivered deep to extensor origin with a peppering technique (2) CSI of 1 mL triamcinolon 40 mg/mL and 2 mL lidocaine 10 mg/mL (3) Placebo injection 3 mL	blinded to injection type Assessors and patients blinded	questionnaire, pain with max grip, quick DASH, modified Nirschl score, MGS, pressure pain threshold PRTEE	4, 12, 26, and 52 weeks	0/60 at 3 months, 34/60 at 6 months, 44/60 at 12 months	ABI for VAS, pain in grip, pressure pain threshold, and Quick DASH (not significant for other outcomes) at 4 weeks and in all outcome measures at 8 weeks CSI superior at 1 month, PRP or CSI not superior to placebo at 3 months with regard to pain reduction. CSI reduces tendon thickness on US more than PRP or placebo	Rash, post-injection pain, skin atrophy, loss of pigmentation	None reported
Wolf, 2011	34 patients with LE, no CSI in prior 6 months	(1) Injection of saline with lidocaine (2) Injection of CS with lidocaine (3) Injection of AB with lidocaine; injections given with multiple passes of needle in fanlike fashion under the extensor origin	Patient but not physician giving injection blinded to injection type	DASH, PRTEE, VAS	2 weeks, 2 and 6 months	6/34 patients lost to follow-up, not included in analysis	There were no statistically significant differences between groups for any outcome measure at any time	None reported	Funded by Clinical Research Grant from the American Society for Surgery of the Hand. No benefits related to the article received
Creaney, 2011	150 patients with LE for at least 6 months failing conservative measures, no previous injection	(1) Injection of PRP (isolated from AB spun in a centrifuge with siphoning of buffy coat layer) (2) Injection of AB; tendons first bathed with bupivacaine before PRP/AB ultrasound guided injection into extensor origin under minimal pressure, second injection given at 1 month (1) Injection of 3 mL AB	Patient and assessor but not investigator blinded to injection type	PRTEE; success defined as an improvement in PRTEE of 25 points at final analysis	1, 3, and 6 months	20/150 lost to follow-up, not included in analysis	At 6 months, both groups experienced a reduction in PRTEE pain scores. The difference in success rate between the 2 groups was not statistically significant. 12/17 patients in the AB group compared to 7/24 patients in the PRP group elected to proceed to surgery	None reported	No competing interests
Thanasas, 2011									

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
	28 patients with LE for at least 3 months	(2) Injection of 3 mL PRP (prepared with Biomet GPS III); injections delivered deep to extensor origin with a peppering technique	Assessors blinded, patients aware of treatment as blood was drawn from ABI group	VAS, Liverpool elbow score	6 weeks, 3 and 6 months	1/28 patients lost to follow-up	Improvement in VAS was larger in PRP group at every follow-up but only the difference at 6 weeks was statistically significant. No significant difference in Liverpool elbow score was noted at any time	With the exception of local pain and discomfort post-injection, no other complications noted	Authors report no conflict of interest
Bracing									
Van De Streek, 2004	43 patients with LE for at least 3 weeks, no CSI in prior month	(1) Thamer Epi-med elbow band (2) Forearm/hand splint (combination of Thamer Epi-med band, orthoflex brace, and aluminum bar from elbow to palm with 30° dorsiflexion at wrist; both groups instructed to wear as much as possible for 6 weeks during all daily activities)	Patient blinding not possible, further blinding not discussed	MGS with pain score (1–10), PRFEQ	6 weeks	3 patients dropped out of study	All outcome measures improved in a statistically significant manner for both groups, there were no statistically significant differences between groups	None	None reported
Garg, 2010	70 patients (74 elbows) with LE, no treatments in prior 6 months	(1) Hely & Weber Velero wrist extension splint (2) Hely & Weber forearm counterforce strap brace; patients instructed to wear brace during all daytime hours for 6 weeks and given standard home icing and stretching exercise	Patient blinding not possible, further blinding not discussed	ASES Elbow Assessment Form derived score, MEP	6 weeks	25 patients lost to follow-up, 3 did not complete outcome measurement forms; 42 patients (44 elbows) included in final analysis	The improvement in the pain component of ASES score was statistically more significant for the wrist extension group at 6 weeks, both groups improved over time but there were no other significant differences in outcome measures	None	No benefits from any commercial entity related to the subject of this article received

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Altan, 2008	50 patients with LE for less than 12 weeks, no prior treatment with CSI or physical therapy during that period	(1) Lateral epicondyle bandage (2) Wrist extension splint; patients instructed to wear braces continuously for 6 weeks, removal for no more than 1 h at a time	Patient blinding not possible; researcher unaware of brace type	VAS pain during rest and with movement, pain with pressure (0–3), grip strength, response to treatment (1, bad, to 4, excellent)	2 and 6 weeks	1/50	Both groups improved in a statistically significant manner over time in all parameters, improvement in resting pain was statistically more significant in the wrist extension splint group at 2 weeks compared to, there was no difference for other parameters between groups at either evaluation	None	This study was not funded by any institution and there are no conflicts of interest
Struijs, 2004	180 patients with LE for at least 6 weeks, no treatment in prior 6 months	(1) 9 physiotherapy (PT) treatments over 6 weeks (pulsed ultrasound, friction massage, strengthening exercises) (2) Eppipoint elbow band worn during the day for 6 weeks	Patient blinding not possible; assessors blinded	Primary: global improvement (1, completely recovered, to 6, much worse), severity of patient's complaints (11-point scale), pain intensity (11-point scale), modified PFFQ Secondary: inconvenience during daily activities (11-point scale), pain-free grip strength, MGS, pressure pain threshold, satisfaction of patient (11-point scale)	6 weeks, 1 year	10/180, included in analysis	No significant differences between groups at 1 year. At 6 weeks, statistically significant benefits of PT over brace were found for pain, disability, and satisfaction. Brace superior only for inconvenience during daily activities. No significant benefit to combination therapy compared to PT, but compared to brace, severity of complaints and satisfaction were statistically significant in favor of combination	None	None reported
Luginbuhl, 2008	35 patients (36 elbows) with LE, no prior treatment with	(3) Combination of above 2 treatments (1) Forearm support band worn during the day for at least 3 months	Patient blinding not possible; no mention	ROM, MGS, Nirschl–Pettrone score	6 weeks, 3 months, and 1 year	6/36 elbows lost to follow-up, not included in analysis; 16 of	All groups had a statistically significant improvement in	None reported	None reported

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
	forearm band or strengthening, no more than 3 CSI in prior 6 months	(2) Strengthening exercises for 3 months (3) Combination of above 2 treatments; all patients initially treated with injection of 2–3 mL Scandicain and 40 mg triamcinolone	assessor blinding			remaining patients did not have follow-up at 1 year but were included in other time points	Nirschl–Pettrone score at 6 weeks and latest follow-up, no significant differences between groups were found at any time point		
Physical therapy									
Peterson, 2011	81 patients with LE for more than 3 months	(1) Daily exercise program for 3 months (2) Wait-and-see	Patient blinding not possible, data collection not blinded	Primary: VAS (during MVC, MME) Secondary: extensor strength, DASH, Gothenburg QOL Instrument	1, 2, and 3 months	2/81, included in analysis	The exercise group had greater and faster regression of pain during MVC and MME than wait-and-see, this difference was statistically significant	Not discussed	Funding sources had no involvement in study. Authors declare no conflict of interest
Park, 2009	31 patients with LE for at least 6 weeks, no CSI in prior 3 months	(1) Immediate physical therapy (2) Physical therapy started after 4 weeks oral NSAIDS	Patient blinding not possible	VAS, modified Nirschl–Pettrone score, MEPS	1, 3, 6, and 12 months	5/31	At 1 month, the difference between groups for the modified Nirschl–Pettrone score and VAS was statistically significant in favor of the immediate therapy group. No other significant differences were found during the study period	Not discussed	Authors declare no conflict of interest
Viswas, 2012	20 patients with LE for 8–10 weeks, no previous therapy	(1) Supervised exercise program (2) Cyriax Physiotherapy; 3 sessions per week for 4 weeks	Patient blinding not possible, assessor blinded	VAS, TEFS	4 weeks	No loss to follow-up	Both groups improved over time, but the group undergoing the supervised exercise program improved more in both outcomes than the Cyriax group, this difference was statistically significant	Not discussed	Authors declare no conflict of interest
Tyler, 2010	21 patients with LE for more than 6 weeks,	(1) Standard physical therapy (2) Standard physical therapy plus isolated	Patient blinding not possible, assessor blinded	DASH, VAS, wrist and middle finger extension	At completion of treatment	No loss to follow-up	Improvements in all outcomes were greater for the eccentric group, this	None	Hygenic Corporation donated flexbars to study.

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
	no CSI in prior 6 weeks	eccentric wrist extensor strengthening (Thera-Band FlexBar); treatments continued until symptoms resolved or patients were referred back to their physician with continued symptoms		strength, pain with pressure			difference was statistically significant		Authors did not receive benefits from any commercial entity related to the article
Martinez, 2005	94 patients with LE for more than 3 months	(1) Stretching plus concentric strengthening program (2) Stretching plus concentric strengthening program (3) Stretching plus eccentric strengthening program	Patient blinding not possible	PPG, PRFEG, DASH, VAS, pain and function assessment with SF-36 patient's subjective assessment of results	6 weeks	13/94, included in intent-to-treat analysis	At 6 weeks, all groups improved in a statistically significant manner for PFG, VAS, DASH, and SF-36. No significant difference was found between groups	Not discussed	Not reported
Extra-corporeal shock wave therapy									
Rompe, 1996	115 patients with LE for more than 12 months, unsuccessful conservative therapy in prior 6 months	(1) ESWT 1000 pulses per treatment (2) Subtherapeutic ESWT; 3 treatments at weekly intervals; no other therapy allowed during course of treatment	Patient and assessor blinded to treatment allocation	VAS, MGS, patient assessed overall outcome (1, excellent, to 4, poor)	3, 6, and 24 weeks after last treatment	15 patients discontinued treatment during first 6 weeks, not included in analysis	In the active treatment group there was a statistically significant decrease in VAS compared to placebo group at each follow-up. There were 24 good or excellent results in the active group compared with only 3 in the placebo group	No complications observed	No benefits received from a commercial party related to the subject of this article
Rompe, 2004	78 recreational tennis players with LE for at least 1 year unresponsive to conservative treatments	(1) ESWT 2,000 pulses per treatment (2) Placebo ESWT with shock waves deflected; 3 treatments at weekly intervals; no other	Patient and assessor blinded to treatment allocation, but 29 of 38 active treatment patients	Primary: VAS during resisted wrist extension Secondary: 50 % reduction in primary outcome measure, Roles	3 and 12 months after last treatment	4 patients withdrew to pursue additional therapy, 2 patients refused follow-up, 2 patients only had phone	At 3 months, the difference in results between treatment groups was statistically significant for all outcome measures, in favor of the active	Temporary reddening after treatment and pain during treatment were common in both groups. 8 patients from the active group and 1 patient	No author or related institution received financial benefit from research study

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Pettrone, 2005	including CSI, no therapy in prior 2 months	therapy allowed during 3 month follow-up	guessed allocation correctly	and Maudsley score (1, excellent, to 4, poor), Upper Extremity Function Scale, grip strength, overall patient satisfaction	1, 4, 8, 12 weeks and 6 and 12 months after last treatment; patients not responding to treatment could be unblinded and placebo patients offered active treatment	6 patients discontinued study prior to 12 weeks, 34 crossover patients considered lost to placebo group, 13 patients discontinued study prior to 12 months; patients included in intention to treat analysis	At 12 weeks, a statistically significant difference between groups was observed for reduction in pain, improvement in upper extremity function, and overall impression of disease state in favor of the active treatment group. Most of the placebo group was lost to crossover at 12 weeks and not available for comparison past this point	from placebo group experienced nausea during treatment	1 or more authors received outside funding from Siemens Medical in support of their research
	114 patients with LE for at least 6 months unresponsive to 2 conventional therapy; no CSI in prior 6 weeks, PT in prior 4 weeks, or NSAIDS in prior week	(1) ESWT 2000 pulses per treatment (2) Placebo ESWT with shock waves deflected; 3 treatments at weekly intervals targeting point of max tenderness	Patients and physicians blinded to treatment allocation	Primary: 50 % reduction of VAS during resisted wrist extension Secondary: Upper Extremity Functional Scale, grip strength, patient overall impression of disease state				Active ESWT: transient treatment-related pain (28), nausea during treatment (10) Placebo ESWT: transient treatment-related pain (13)	
Haake, 2002	272 patients with LE, at least 6 months unsuccessful conservative therapy and no treatment prior 2 weeks	(1) ESWT 2,000 pulses per treatment (2) Placebo ESWT with shock waves deflected; 3 treatments received, injection of 3 mL 1 % mepivacaine administered before each treatment	Patients and assessor blinded to treatment allocation	Primary: success rate after 12 weeks (defined as score of 1 or 2 on Roles and Maudsley score and no additional treatment during study period) Secondary: Roles and Maudsley score, VAS, MGS	6 and 12 weeks after last treatment	26/272, included in intention to treat analysis	There were no significant differences between groups in any outcome measure at any time	No severe adverse events noted. Most common side effects were reddening of skin (42 ESWT, 11 placebo) and pain (15 ESWT, 6 placebo)	Domier Medizintechnik provided shock wave equipment. Benefits were directed to an institution with which 1 or more authors are associated

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Speed, 2002	75 patients with LE for at least 3 months, no treatment in prior 6 weeks	(1) ESWT 1,500 pulses per treatment with Sonocor Plus Unit (Siemens) (2) Placebo ESWT, subtherapeutic doses without skin contact; 3 treatments at monthly intervals directed to site of maximum pain; no other treatments permitted during study	Patients and assessor blinded to treatment allocation	VAS	1 month after last treatment	4 patients withdrew from study	Both groups had statistically significant improvement over time, no significant differences existed between groups at any time	2 patients in active treatment group withdrew due to worsening symptoms, no other adverse effects reported	Funded by Cambridge Arthritis Research Endeavour
Melikyan, 2003	86 patients with LE who had received extensive conservative treatment and were awaiting surgery	(1) ESWT starting at a low energy and gradually increased, total of 1,000 mJ/mm ² energy delivered (2) Placebo ESWT with shock waves deflected; 3 treatments targeting common extensor tendon under ultrasound guidance	Patient and assessor blinded to treatment allocation	DASH, MGS, analgesic requirement	1, 3, and 12 months after last treatment	12/86, not included in analysis	None of the outcome measures showed a statistically significant difference between groups at any time. All patients improved significantly over time	None reported	Supported by BUPA research fund. Benefits received from a party related article are directed to a research fund or other non-profit institution with which 1 or more authors associated
Chung, 2005	60 patients with untreated LE for between 3 weeks and 1 year	(1) ESWT 2,000 pulses, 0.03–0.17 mJ/mm ² energy delivered (2) Placebo ESWT with shock waves deflected; 3 treatments at weekly intervals targeting point of maximum pain, all patients provided a stretching protocol	Patient and assessor blinded to treatment allocation	VAS (overall pain, resting pain, pain during sleep, pain during activity, pain at its worst, pain at its least), QOL on EuroQol 5D instrument (EQ5D), max PFGS, pain medication used (success defined as 50 % reduction in overall elbow pain, max overall elbow pain of 4 cm, and no use of	4 and 8 weeks after last treatment	1 patient dropped out of study, 3 were lost to follow-up, included in intention to treat analysis	At 8 weeks, there was no statistically significant difference in success rate between treatment groups	No severe or moderate adverse events were observed	Funded by Sport Science Association of Alberta and Alberta Provincial Canadian Institutes of Health. No author received financial benefit from research in this study

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Staples, 2008	68 patients with LE for at least 6 weeks, no oral/topical NSAID in prior 2 weeks, or oral CS in prior 6 weeks	(1) ESWT 240 pulses/min, 2,000 pulses per treatment (2) Subtherapeutic ESWT; 3 treatments at weekly intervals targeting area of maximal tenderness over common extensor tendon; no other forms of therapy including NSAIDs allowed during first 6 weeks of study	Patient and assessor blinded to treatment allocation	VAS (pain, function), discomfort in daily activities, DASH, QOL using Medical Outcome Study SF-36, max PFG, Problem Elicitation Technique	6 weeks, 3 months, and 6 months after completion of 3-week treatment	2 patients withdrew after treatment, 3 patients did not attend 6-week follow-up, 3, did not attend 3-month follow-up, and 5 did not attend 6-month follow-up; all patients included in intention to treat analysis	There were no significant differences between groups in any outcome measures at 6-week and 6-month follow-up visits. At 3 months, there was a statistically significant difference between groups in favor of the active group for DASH (work and sport), but neither section was completed by all patients	Active ESWT: bruising after 1st treatment (1), pain/tenderness in arm (4), burning sensation (1) Placebo ESWT: pain and/or lump in treated area (2)	Supported by Australian National Health and Medical Research Council Practitioner Fellowship.
Laser									
Lundeberg, 1987	57 patients with LE for at least 3 months, no CSI in prior 6 months	(1) Placebo laser (2) Ga-As pulse laser, 904 nm wavelength (3) He-Ne continuous-wave laser, 632.8 nm wavelength; 2 treatments per week given over 5 to 6 weeks with laser stimulating 10 acupuncture points	Patients, therapists, and assessors blinded to laser type	VAS, pain and power with resisted wrist dorsiflexion (0, no pain, to 3, severe pain and absent power), wrist extension strength, grip strength, patient and physician assessment of treatment (satisfactory/unsatisfactory)	Every other week during treatment and at least 3 months after treatment	Not discussed	The 3 treatment groups showed no significant difference in any outcome measure at any time	None reported	Work supported by grants from The Royal Swedish Academy of Sciences and Stiftelsen Clas Groschinsky minnesfond
Haker, 1990	49 patients with LE for at least 1 month	(1) Ga-As Mid 1500 IRRADIA laser, wavelength 904 nm (2) Placebo laser: 10 treatments, 2–3 times weekly targeting the extensor group of muscles	Patients, therapist, and assessors blinded to laser type	Subjective physician assessment (1, excellent, to 5, unchanged or worse), max pain free grip	After last treatment and 3 months post-treatment, 1 year follow-up with questionnaire	2 patients withdrew after treatment, 7 additional patients withdrew after 3 months follow-up	At 3 months, there were no significant differences between treatment groups for any outcome measure	None reported	Work supported by grants from Foundations of Karolinska Institutet

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Krasheninnikoff, 1994	48 patients with LE for at least 1 month, no CSI in prior 3 weeks or other simultaneous treatment	(1) Active Ga–Al–As laser (30 mW/830 nm) (2) Placebo laser: 8 treatments 2 times per week targeting tender points on lateral epicondyle and in forearm extensors	Patients, therapists, and assessors blinded to laser type	Duration of pain, pain relief, symptoms, patients subjective impression of effect	Telephone interview at 10 weeks post-treatment	12/48; excluded from analysis	At 10 weeks, there were no significant differences between treatment groups for any outcome measure	None reported	None reported
Papadopoulos, 1996	29 patients (31 elbows) with LE	(1) Ga–Al–As laser (50 mW/820 nm) (2) Placebo laser: 3 treatments per week for 2 weeks targeting most tender point	Patients, operator, and assessor blinded to treatment	VAS, pain threshold with exercising forearm extensors	1st, 4th, and 6th treatment visit	No loss to follow-up	There were no statistically significant differences between groups for any outcome measure at any time	None reported	Loan of equipment by Omega Technologies
Vasseljen, 1992	30 patients with LE, no other treatments in prior 3 weeks	(1) Ga–As laser (18 mW/904 nm) (2) Placebo laser: no other treatments allowed during study; 8 treatments were given at a frequency of 3 times per week	Patients, operator, and assessor blinded to treatment	MGS, extension weight test, point of pain with wrist flexion, VAS, patient subjective assessment of improvement	Post-treatment and 4 weeks after last treatment	1 patient had alternative treatment during study, dropped and was replaced by another patient	Statistically significant improvement in laser compared to placebo was found for VAS and MGS 4 weeks after treatment	Not discussed	Supported by grant from Norwegian Fund for Post-Graduate Education in Physiotherapy. Schreuder Instrumenten supplied lasers
Basford, 2000	47 patients with LE for more than 30 days, no CS administered for any reason in prior 30 days	(1) Nd:YAG CW 1.06 μm continuous wave laser (204 mW/cm ²) (2) Inactive laser: 3 treatments per week for 4 weeks targeting 7 points along the symptomatic forearm	Patient, therapist, and physician blinded to laser type	Primary: VAS for max pain in last 24 h, max tenderness on palpation, and patient perception of change Secondary: grasp and pinch strength, pain with grasp and pinch	1st, 6th, and 12th treatment visit and 1 months post-treatment	1 patient did not return for 1 months follow-up	There were no statistically significant differences between groups for any outcome measure at any time	No significant treatment side effects were noted	Authors have not received a benefit from any commercial party having a direct financial interest in the results of the research supporting this article
Stergioulas, 2007	62 patients with LE for at least 5 weeks, no treatment in prior month	(1) Ga–As continuous wave laser (40 mW, 904 nm) plus plyometric exercises (2) Placebo laser plus plyometric exercise, 12 treatments over 8 weeks	Patients and physical therapist performing assessments blinded to laser type	VAS (pain at rest, with palpation of lateral epicondyle, during resisted extension), ROM, grip	Post-treatment and 8 weeks after last treatment	12/62 patients left study to pursue other treatments	Relative to the placebo group, the active treatment group had a statistically significant decrease in pain at rest, with palpation, during resisted middle finger	No complications reported by patients	None reported

Table 1 (continued)

Author, year	Participants	Experimental groups	Blinding	Outcome measures	Follow-up periods	Lost to follow-up	Results	Side effects (number of patients affected)	Conflict of interest statement and/or source of funding
Corticosteroid injection									
Lam, 2007	39 patients with LE, no previous episode of lateral elbow pain on same side or any prior treatment	(1) Ga–As laser (25 mW, 904 nm) plus exercise program (2) Placebo laser plus exercise program; 3 treatments per week for 3 weeks targeting all tender points	Patient and physician blinded	strength, and free weight test Mechanical pain threshold, MGS, VAS, DASH	5th and 9th treatment session and 3 weeks post-treatment	Not discussed	extension, and during grip strength testing and an increase in grip strength and weight testing at both follow-up intervals A statistically significant difference in improvement for all outcome measures were found between the laser group and the placebo group in favor of the active laser group, except in 2 subsections of DASH	None reported	None reported
Emanet, 2010	49 patients (50 elbows) with LE for less than 3 months, no PT or CSI in prior 2 months	(1) Ga–As laser (100 W/905 nm) with exercise program (2) Placebo laser with exercise program; 5 treatments a week for 3 weeks targeting the 2 most sensitive points around the lateral epicondyle	Patients and assessor blinded to laser type	VAS, pain with pressure over lateral epicondyle, DASH, PRTEE, pain free grip strength, Nottingham Health Profile (NHP)	3 and 12 weeks	3/49, excluded from analysis	At 3 weeks, a statistically significant improvement in all outcomes was observed in both groups. At 12 weeks, a statistically significant improvement in favor of the active laser group was found for pain with resisted wrist extension, pain with pressure, DASH, PRTEE, and NHP (pain)	None reported	No competing financial interests exist

AB autologous blood, ASES American Shoulder and Elbow Society, CSI corticosteroid injection, ESWT extra-corporeal shock wave therapy, LE lateral epicondylitis, MEPS Mayo Elbow Performance Score, MGS maximum grip strength, MME maximum muscle elongation, MPFGS Maximum Pain Free Grip Score, MVC maximum voluntary contraction, PFFQ Pain Free Function Questionnaire, PFG pain free grip, PRFEQ Patient Rated Forearm Evaluation Questionnaire, PRP platelet-rich plasma, PRTEE Patient Rated Tennis Elbow Evaluation, PT physiotherapy, QIVAS Quadruple Visual Analogue Scale, QOL quality of life, ROM range of motion, SF-12 Short Form 12, SF-36 Short Form 36, TEFS Tennis Elbow Function Score, VAS Visual Analogue Scale (for pain unless otherwise specified)

Significant ($p < 0.001$) decreases in pain were seen with both drugs after one treatment a day for up to 18 days. Sodium diclofenac produced a larger reduction in pain than sodium salicylate. A RCT of oral diclofenac and placebo was conducted by Labelle and Guibert [28]. Both groups were immobilized and the treatment group received 150 mg of diclofenac daily for 28 days. No difference was found between the groups with regard to function; however, there was a significant ($p < 0.03$) difference in pain reduction in the treatment group.

In Nirschl et al. [40], patients received six treatments of dexamethasone or placebo iontophoresis within 15 days. At 2 days post-treatment, those treated with dexamethasone reported significantly ($p < 0.012$) less pain on VAS than patients receiving placebo. There was no significant ($p = 0.249$) difference found between the groups at 1 month.

Stefanou et al. [57] tested the delivery of dexamethasone via a self-contained battery powered iontophoresis patch against dexamethasone injection and triamcinolone injection. All subjects also received therapy. Outcomes were assessed at the end of therapy and at 6 months. Outcomes were similar for all groups at 6 months, but only the iontophoresis group had significantly ($p < 0.05$) improved grip strength and higher rates of returning to work without restriction at the end of therapy.

Botulinum Toxin A Injection

Botulinum toxin A has been proposed as a non-surgical option for treatment of lateral epicondylitis. The mechanism for relief of pain is paralysis of extensor muscles, preventing further microtrauma to the tendon origins and allowing healing to occur.

Hayton et al. [24], Wong et al. [69], Placzek et al. [47], and Espandar et al. [18] compared 50–60 U of botulinum toxin A or saline injected 1–5 cm distal to the point of maximum tenderness or one third the distance along the forearm from the tip of the lateral epicondyle. Primary outcomes were pain score and grip strength at intervals up to 18 weeks. Hayton's group did not find any difference between the treatment and placebo groups at any time. However, studies by Wong, Placzek, and Espandar found significant ($p < 0.006$, 0.003, and 0.01, respectively) differences in pain score but not in grip strength. All studies documented patients in the treatment groups who experienced transient weakness in finger extension.

Lin et al. [30] compared botulinum toxin A to corticosteroid injection and assessed VAS pain score, quality of life, and grip strength at 4, 8, and 12 weeks. The botulinum treatment was significantly ($p < 0.02$) less effective in reducing pain and resulted in significantly ($p < 0.01$) reduced grip strength when compared to the corticosteroid group at 4 weeks. The reduced grip strength continued at 8 weeks. There was no difference in quality of life at any time.

Prolotherapy

Prolotherapy consists of an injection composed of osmotics/irritants (dextrose or polidocanol) and/or chemotactics (sodium morrhuate), which promote inflammation in the target tissue. The iatrogenic local inflammation is proposed to induce fibroblastic growth and collagen synthesis, ultimately leading to stronger repair of damaged fibers at the lateral epicondyle.

A double-blind RCT was performed by Scarpone et al. [52] to assess the efficacy of prolotherapy vs. placebo injection in the treatment of refractory lateral epicondylitis. The study group received three injections of dextrose, sodium morrhuate, lidocaine, and sensorcaine at 4-week intervals, while the control group received saline injections. Significantly ($p < 0.05$) improved pain and grip strength were observed in the prolotherapy group at intervals up to 52 weeks.

Carayannopoulos et al. [8] compared prolotherapy and corticosteroid injections for the treatment of lateral epicondylitis in a later RCT. The prolotherapy group received two injections consisting of dextrose, glycerin, phenol, sodium morrhuate, and procaine, whereas the corticosteroid group received an injection of methylprednisolone and procaine. Both groups demonstrated significant ($p < 0.04$) improvement at 3 or 6 months, but results of this study did not include the 29 % of patients with inadequate follow-up. No difference could be found between the treatments. Zeisig et al. [70] studied ultrasound guided injections of polidocanol vs lidocaine/epinephrine in a double-blind RCT and reported improvement in grip strength and VAS in both groups at 3 months with no difference between groups.

Platelet-Rich Plasma and Autologous Blood Injection

Injections of PRP or ABI have been proposed to facilitate healing through release of growth factors directly at the site of interest. Specifically, PRP contains high levels of various growth factors including platelet-derived growth factor, transforming growth factor beta, and vascular endothelial growth factor [35]. PRP is created by withdrawing the patient's own blood and centrifuging it to isolate a platelet-rich fraction before injecting into the patient at the site of interest. In the case of ABI, autologous blood is withdrawn from the patient but is not treated before reinjection.

Several studies have compared the injection of PRP or ABI to injection of corticosteroids. Gosens et al. and Peerbooms et al. [20, 44] performed double-blind RCTs demonstrating a significant ($p < 0.005$) difference in favor of the groups receiving PRP injections over those receiving corticosteroid injections with follow-up intervals up to 2 years. Similarly, Kazemi et al. [25] compared ABI to corticosteroid injection in a RCT where assessors were unaware of treatment. At 8 weeks, ABI was found to be more effective in all outcomes. A recent study

by Krogh et al. [27] did not find PRP superior to corticosteroid injection at 1 month or to either corticosteroid injection of placebo at 3 months of follow-up; however, tendon thickness was found to be reduced on ultrasound examination in corticosteroid injection over PRP or placebo test subjects.

Wolf et al. [68] attempted to account for any placebo effect associated with injection by adding a control group to their RCT study design. Patients were randomized to receive one of three treatments including ABI, corticosteroid/lidocaine injection, and saline/lidocaine injection. Outcomes improved over time in all three groups with no differences at 2- and 6-month follow-ups.

PRP has also been compared directly to ABI. Creaney et al. [14] conducted a double-blind RCT with patients receiving injections at 1 month intervals of either autologous blood or PRP. Both preparations produced improvement over 6 months, but there were no differences between groups. Thanasis et al. [61] also compared the two in a RCT in which assessors were unaware of treatment allocation. Ultrasound guidance and peppering injection technique was used in both groups. Statistically significant ($p < 0.05$) improvement in pain for PRP over ABI was present only at 6 weeks.

Bracing

Two commonly used braces are the proximal forearm strap (counter force brace) and wrist extension splint. By holding the wrist in extension, the splint is thought to unload the extensor origin and relax the wrist extensors. There are several theories as to how the forearm strap reduces the force exerted on the common extensor origin, one being that its compressive force limits expansion and thereby the force generated by the extensors. Another is that the strap serves as a secondary origin for the ECRB muscle, reducing the force conducted proximally [39]. Both mechanisms would theoretically decrease stress on the damaged tendons, allowing healing.

Several authors have compared the effects of the proximal forearm strap and wrist extension splint on lateral epicondylitis symptoms. One study found no difference between the two orthotics [64], and two found a substantial difference in favor of the wrist splint in reduction of pain [2, 19]. Both studies were limited to 6 weeks of follow-up and lacked a control group; one study [19] did not include 40 % of patients with inadequate follow-up, making interpretation of the true benefit of either splint difficult to determine in these studies.

Struijs et al. [59] randomly assigned 180 patients to forearm strap, physical therapy, or combination and found no differences at 26- or 52-week follow-ups. At 6 weeks, the strap-only group was significantly ($p < 0.05$) better in ability to perform daily activities. Luginbuhl et al. [32] compared use of a forearm strap for at least 3 months, strengthening exercises, and a combination with the addition of a corticosteroid

injection at the beginning of treatment. All groups experienced significant ($p < 0.0001$) improvement in pain at 6 weeks and 1 year, and there was no difference between groups at any time.

Physical Therapy

PT is often employed for non-surgical treatment of lateral epicondylitis. There are many studies comparing the efficacy of PT to other modalities of treatment that are included elsewhere in this review. There are also several RCTs which have compared PT to wait-and-see or examined different methods of PT. Peterson et al. [45] and Park et al. [43] compared PT to wait-and-see, with mixed findings. Peterson's group found significant ($p < 0.0016$) improvement in pain for the treatment group while Park saw significantly ($p < 0.01$) better pain scores for the control group. Viswas et al. [67] evaluated a stretching/strengthening program against Cyriax friction massage, finding no difference in outcomes between the methods. Tyler et al. [63] and Martinez-Silvestrini et al. [34] examined various combinations of eccentric and concentric exercises compared to standard PT with inconsistent results; Tyler's study found a significant difference ($p < 0.011$) in all measures for the eccentric group while Martinez-Silvestrini found no difference in outcomes between any group. The recent study examining corticosteroid injection and physical therapy by Coombes et al. [11] previously discussed found short-term improvement with physical therapy alone; however, this effect disappeared by 26 and 52 weeks of follow-up.

Shockwave Therapy

Extracorporeal shock wave therapy (ESWT) applies energy to the interface of two substances with differing acoustic impedance. It has been proposed that this energy promotes tissue healing and possibly reduces pain by stimulating nerve fibers to produce analgesia [56].

Of the several double-blind RCTs done to evaluate the efficacy of ESWT, only two authors have produced significant ($p < 0.001$) findings. Rompe et al. conducted two studies [50, 51] looking at the efficacy of ESWT in the treatment of lateral epicondylitis. Both studies were double-blind RCTs looking at patients with refractory lateral epicondylitis of at least 12 months. Patients received three weekly treatments of either active or sham ESWT. In the earlier study, significant ($p < 0.001$) improvement in pain and grip strength was observed in the active treatment group at 3, 6, and 24 weeks. In the later study, significant ($p < 0.001$) difference in favor of the active treatment group was found up to 12 months after treatment. Pettrone and McCall [46] also saw a positive effect of ESWT on pain and function 12 weeks post-treatment in patients with refractory lateral epicondylitis for more than 6 months. Other investigators, Haake et al. [21], Speed et al.

[55], Melikyan et al. [36], Chung et al. [10], and Staples et al. [56] did not find any substantial difference between treatment and placebo groups with any outcome measure.

Laser Therapy

Low-level laser therapy (LLLT) is proposed to have a biostimulatory effect on tissue, reducing levels of TNF alpha [1] and reducing cell apoptosis [9] although the precise method by which this occurs is incompletely understood. The effect of LLLT on lateral epicondylitis has been studied with conflicting results. Early double-blind RCTs did not show an advantage to LLLT. Lundberg et al. [33] studied two different types of laser (pulsed Ga–As and continuous He–Ne), with no difference between treatment and placebo groups up to 3 months after treatment. Four more RCTs studied the effect of either a Ga–As or Ga–Al–As laser vs. sham laser therapy. Varying levels of energy were delivered per point in each study, and follow-up periods ranged from 7 weeks to 1 year. Three studies did not demonstrate a difference in results between laser therapy and placebo [22, 26, 42] (although one of these studies [26] did not include 25 % of subjects lost to follow-up) whereas a fourth study did [65].

Results of more recent studies conflict with those found previously. Basford et al. [4] conducted a double-blind RCT with a Nd-YAG laser and placebo which did not demonstrate a difference in outcome at 4 weeks. However, a study by Stergioulas [58] combined plyometric exercise with Ga–As laser or placebo laser and found a significant ($p < 0.05$) improvement in VAS and strength at 8 and 16 weeks in the active treatment group. A similar study by Lam and Cheing [29], looking only at short-term outcomes of Ga–As laser treatment at 3 weeks found comparable results ($p < 0.0125$). Emanet et al. [17] also found positive results of LLLT in their double-blind RCT using a Ga–As laser and additional physical therapy for both groups with a statistically significant ($p < 0.05$) difference with respect to improved pain, grip strength, and functional assessment in favor of the treatment group at 12 weeks.

Discussion

Many non-surgical treatments for lateral epicondylitis have been developed and studied. Corticosteroid injection, injection technique, iontophoresis, botulinum toxin A, prolotherapy, platelet-rich plasma/autologous blood injections, bracing, physical therapy, extracorporeal shock wave therapy, and laser therapy have been subjected to RCTs. When taken in aggregate, we propose there are several conclusions to be drawn from the collection of studies reviewed herein.

Given that lateral epicondylitis is thought to result from repetitive microtrauma, rather than an inflammatory process,

it is not surprising that corticosteroid injections do not provide long-term relief. Patients receiving corticosteroid injections have improved pain relief over physical therapy or a wait-and-see approach for 1 to 2 months post-treatment, although these effects do not remain when examined at 1 year. The several studies testing the effect of a peppering technique of corticosteroid injection show the technique improves results at 6 months to 1 year of follow-up. RCTs of iontophoresis have shown some benefit to this technique of corticosteroid delivery, at least on a very short-term basis of days to weeks.

Other types of injection have been studied in addition to injection of corticosteroids. Treatment with botulinum toxin A may also provide pain relief when compared to placebo, but not to corticosteroid injection, and the accompanying transient extensor weakness may not be acceptable to patients. Prolotherapy is superior to saline placebo but does not appear to be more effective than corticosteroid or lidocaine injection. PRP and ABI have been found to be both less and more effective than corticosteroid injections, and PRP has been shown to also be either more or equally effective than ABI in studies.

Bracing with a proximal forearm strap or wrist extension splint, however, seems to provide little to no additional benefit when combined with physical therapy. The studies reviewing physical therapy without bracing or other concurrent treatment did not show a clear advantage to PT.

Non-invasive techniques such as laser therapy and ESWT have been the subject of RCTs. Early studies of laser therapy did not show an effect of treatment whereas more recent investigations did show substantial improvement for patients treated with laser therapy over those who received placebo therapy. These beneficial effects were most apparent at 1 to 4 months of follow-up. The preponderance of studies of extracorporeal shockwave therapy appears to indicate that this treatment is no more effective than placebo.

A weakness of this systematic review is that which is inherent in many studies, even those which are undertaken as RCT, blinded trials: Design of the perfect trial is probably impossible, as there are always unanticipated variables [13]. Patients are lost to follow-up, have subjective responses to test criteria, or there may be unintended investigator bias. However, given a large number of investigations, valuable conclusions may be drawn.

In summary, lateral epicondylitis is a condition that is usually self-limited, resolving over a 12- to 18-month period without treatment. There are many options for non-surgical treatment for pain relief. Corticosteroids, whether delivered with a standard or peppered injection technique or via iontophoresis, may provide short-term pain relief on the order of several months; however, this effect is not sustained in the long term. Injections of botulinum toxin A, prolotherapy, PRP, or ABI may also provide varying degrees of improvement in pain, although botulinum toxin A can have unacceptable side

effects. Studies of LLLT do not show a clear benefit at this time. Therapies that do not include injection, such as bracing, PT, or ESWT, do not appear to provide substantial benefit in terms of pain relief or improved function. In conclusion, there are multiple randomized controlled trials for non-surgical management of lateral epicondylitis, but the existing literature does not provide conclusive evidence that there is one preferred method of non-surgical treatment for this condition.

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