Injection of Botulinum Toxin for Treatment of Chronic Lateral Epicondylitis: Systematic Review and Meta-Analysis

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Objectives: Lateral epicondylitis can be chronic and difficult to manage with conservative measures such as physical therapy and corticosteroid injection. We attempted to determine the efficacy of botulinum toxin for the treatment of chronic lateral epicondylitis.

Methods: We searched PubMed, MEDLINE, CINAHL, Google Scholar, EMBASE, PEDro, and ISI web of Science databases from inception until November 2009. Studies were included if they used any formulation of botulinum toxin A for treatment of chronic lateral epicondylitis and reported at least 1 pain outcome. One author extracted the relevant data using a standardized data extraction sheet and a second author checked the data. We performed a meta-analysis by computing effect sizes for each study separately for pain and grip strength at 3 months after injection. Impact of bias was assessed independently by 2 authors.

Results: The search found 10 studies relevant to the question. Four of these were randomized controlled trials that could be pooled in a meta-analysis. Results showed a moderate effect for pain favoring botulinum toxin (effect size −0.5, 95% CI −0.9, −0.1, $I^2 = 56\%$) at 3 months and a no effect for grip strength. Qualitative analysis of the studies that could not be pooled also showed improvement in pain, but was limited by potential bias.

Conclusions: Present literature provides support for use of botulinum toxin A injections into the forearm extensor muscles (60 units) for treatment of chronic treatment-resistant lateral epicondylitis. It is minimally invasive and can be performed in an outpatient setting.

 Semin Arthritis Rheum 40:532-538

Keywords: *tennis elbow, lateral epicondylitis, botulinum toxin A, treatment, meta-analysis*

Lateral epicondylitis (tennis elbow, radial epicondylitis, lateral epicondylalgia) is a frequent complaint in primary care and is considered to be an overuse injury, affecting the common extensor tendon close to its attachment at the lateral humeral epicondyle. The tendons involved are responsible for anchoring the muscles that extend or lift the wrist and hand.

Lateral epicondylitis is the most commonly diagnosed elbow affliction. Its prevalence is 1 to 3% of the general population and 15% of workers in at-risk industries (1-4). Its incidence is estimated at 4 to 7 per 1000 patients per year in general practice (5). Peak incidence is at 40 to 50 years of age, and for women age 42 to 46 years the incidence increases to 10% (6). In addition to patient morbidity, lateral epicondylitis is also an economical burden in western societies, resulting in sick leave and absenteeism. In the Netherlands approximately 16% of patients treated by general practitioners required medical leave, with a mean sick leave of 9.3 weeks (7).

Medical practitioners utilize various conservative treatments for lateral epicondylitis, including a wait-and-see policy, special bandages, immobilization in a cast for several weeks, nonsteroidal anti-inflammatory drugs, extracorporeal shock wave therapy, corticosteroid injection, and different physiotherapeutic methods. Recent evidence (8,9) has shown that corticosteroid injections are

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The authors have no conflicts of interest to disclose.
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 0049-0172/11/$-see front matter
doi:10.1016/j.semarthrit.2010.07.002

superior to wait-and-see or physical therapy in terms of success rates and pain-free grip index at 3 and 6 weeks after the injection. However in the long term (6 and 12 month after injection), individuals from wait-and-see or physical therapy groups showed better results than those from the corticosteroid group (8).

In 1997 botulinum toxin A was introduced for treatment of various musculoskeletal conditions (10,11). Several studies have had promising outcomes for the treatment of lateral epicondylitis after botulinum toxin A injections (12-14). We performed a systematic review of all available studies with an emphasis on randomized controlled trials (RCT) to determine whether injection of botulinum toxin can be a viable treatment for chronic lateral epicondylitis.

METHODS

Search Strategy

PubMed, MEDLINE, CINAHL, Google Scholar, EMBASE, PEDro, and ISI web of Science databases were searched from inception until November 2009 for the key words "elbow," "lateral," "epicondylitis," "tennis elbow," "epicondylalgia," "treatment," "injections," "Botox," "Dysport," and "botulinum." The titles and abstracts of all articles were reviewed. The search was initially run by 1 reviewer (L.K.) and then it was repeated by 2 reviewers (R.B. and W.H.). The last full search was run on November 3, 2009. Criteria for inclusion in the review were use of any formulation of botulinum toxin A for treatment of lateral epicondylitis and reporting of at least 1 pain outcome. Trials of any methodological quality were included.

Types of Studies

We analyzed all published material with an emphasis on RCTs. No language restrictions were imposed. Foreign language papers were translated. The reference lists of all articles retrieved in full were also searched. In addition, we consulted orthopedic and rheumatology experts to produce this systematic review and meta-analysis on the effect of botulinum toxin injections on lateral epicondylitis symptoms.

Data Extraction

We developed a data extraction sheet and tested it on 3 randomly selected included studies and refined it accordingly (15). One author (R.B.) has extracted the relevant data from included studies and second author (W.H.) checked the extracted data. Disagreements were resolved by discussion between the 2 authors; if no agreement could be reached, it was planned a third author (L.K.) would decide. We contacted 1 author for further information and he provided additional numerical data, which was not presented in the published paper (12).

Data Items

Information was extracted from each included trial on the following: (1) characteristics of trial participants (including age, sex, stage and severity of disease, duration of disease); (2) type of intervention (including type, dose, duration, and frequency of Botulinum toxin versus placebo); (3) type of outcome measure (including the level of pain reduction, grip strength).

Assessment of Risk of Bias

Two authors (R.B., W.H.) working independently, in a blinded manner and with adequate reliability, ascertained the validity of eligible randomized trials. They determined the adequacy of randomization, allocation concealment, blinding of patients, health care providers, data collectors, outcome assessors, and extent of withdrawals and type of analysis performed (whether intention-to-treat or not). The case series were assessed based on an adaptation of the Newcastle–Ottawa Quality Scale for case control studies. This tool prompts for assessment of adequacy of case definition, representativeness of cases, and ascertainment of the exposure (in this case description of the intervention) (16). Because they are case series, other quality measurements in the Newcastle–Ottawa Quality Scale are not met (selection and definition of controls, comparability of cases and controls, and nonresponse rates for cases and controls).

Statistical Methods

We performed a qualitative analysis on the studies that could not be pooled and a meta-analysis for the 4 RCTs. We computed effect sizes for each study separately for pain and grip strength at 3 months after injection (the only time point used consistently in all studies). We calculated Hedges' g score for each study as a measure of effect size. To correct for small sample size bias, we computed the bias-corrected Hedges' g score for each measure (17). In view of significant heterogeneity, DerSimonian and Laird's method of random-effect models was used for pooling (18). Heterogeneity was estimated with the I^2 statistic for both RCTs and case series (19). I^2 values of 25%, 50%, and 75% corresponded to low, moderate, and high between-trial heterogeneity. All analyses were conducted using Meta-Analyst version 3.13 statistical software (Tufts Medical Center, Boston, MA) (20).

RESULTS

Trials

Our search yielded 874 articles. An additional newly published study was identified by hand search after the initial submission of this article. After review of the title and abstracts, 19 references considered as potentially relevant were reviewed in full. After full review, 9 articles were excluded since they were not relevant to the study ques-

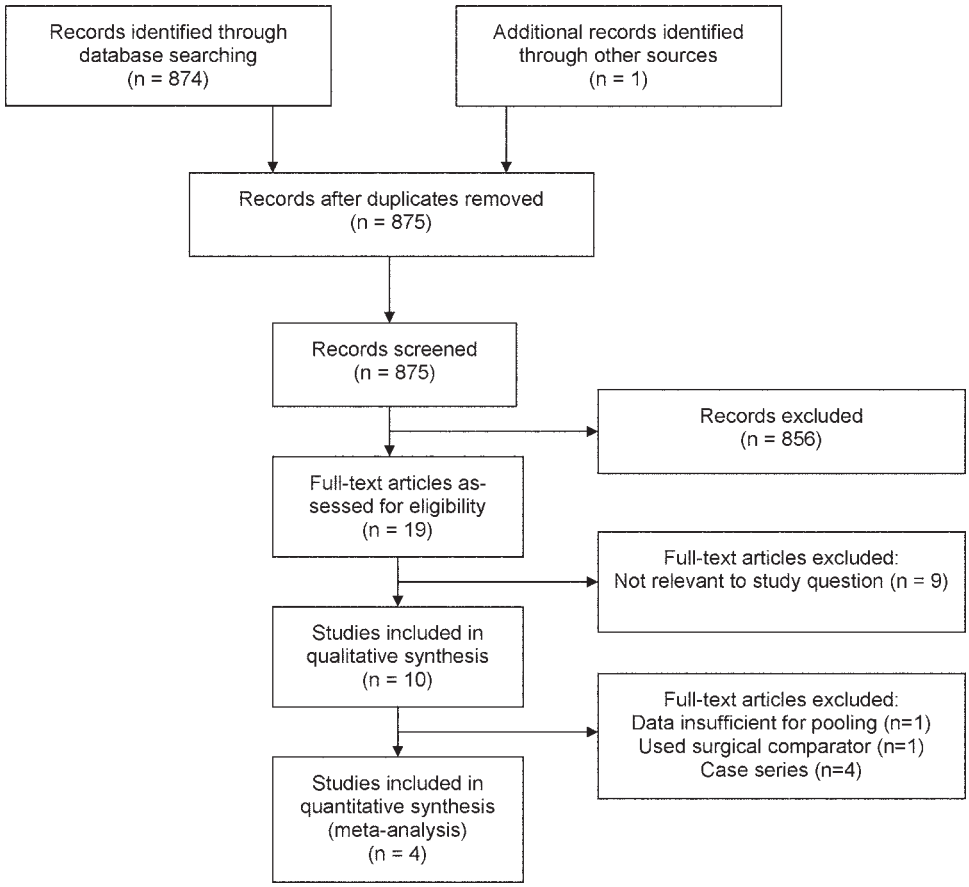

Figure 1 Summary of the search results and study selection.

tion. Several articles did not include sufficient data for pooling. One author provided additional data not available in the article, but used surgery as the comparator arm and was excluded from the meta-analysis (12). Three did not report any continuous outcome measures for pain (21-23). Four were case series that did not contain a comparator group (22-25). Therefore, our meta-analysis was based on 4 studies (13,14,26,27) (Fig. 1). We report a qualitative summary of the 6 studies that could not be pooled, followed by details of the studies included in the meta-analysis.

Qualitative Analysis of Excluded Studies

The systematic review yielded 6 studies that could not be pooled in the meta-analysis. Two case series (24,25) used a VAS pain scale (0-100) to evaluate participants before and after botulinum toxin injection. The results for both showed a statistically significant improvement in pain following injection. Because these studies were not blinded and had no comparator group, they were not included in the meta-analysis. Another open case series reported improvement, but did not provide any data (22). One additional case series (28) was published as an abstract and reported results of improvement VAS scale, but did not provide the data. Another study simply reported improvement versus no improvement (23). The final study was a RCT comparing botulinum toxin to modified surgical release and showed no significant benefit for either group (12). This study was also not blinded. The author provided results of VAS pain scores that were not reported in the original article; however, the surgical comparator arm precluded its inclusion in the meta-analysis.

Qualitative and Quantitative Analysis (Meta-Analysis)

Trial Characteristics

The characteristics of the 4 included studies are shown in Table 1, and the characteristics of the participants involved are shown in Table 2. These studies were published between 2004 and 2010. They comprised 4 RCTs (13,14,26,27). Overall, these studies included 273 participants, with 143 receiving botulinum toxin A and 130 receiving placebo. The mean age range for included participants was 43 to 48 years. All studies defined chronic lateral epicondylitis as a disease duration of at least 3 months and a combination of local tenderness at the lateral epicondyle and pain with resisted extension of the wrist and/or third finger.

Of the 4 RCTs, 3 (13,14,26) used 60 units of botulinum toxin A (Dysport formulation) and 1 (27) used 50

Table 1 Characteristics and Risk of Bias of the RCTs

Study (Type)	Dose of Botulinum Toxin A	Allocation Sequence Adequately Generated	Blinding	Allocation Concealment	Intent to Treat	Were Outcome Measures Reliable
Wong et al., 2005 (14) (RCT)	60 units Dysport	Yes (block randomization)	Double	Yes	Yes	Yes
Hayton et al., 2005 (27) (RCT)	50 units Botox	Yes (block randomization)	Single evaluator	Yes	No	No
Placzek et al., 2007 (13) (RCT)	60 units Dysport	Yes (block randomization)	Double	Yes	Yes	Yes
Espandar et al., 2009 (26) (RCT)	60 units Dysport	Yes (block randomization)	Double	Yes	Yes	Yes

units of botulinum toxin A (Botox formulation). All 4 used saline as a control.

The location of the injection varied between studies. Among the RCTs, in 1 study (13) botulinum toxin A was injected 3 to 4 cm distal to tender lateral epicondyle; in the second study (14) it was injected 1 cm distal to lateral epicondyle toward the point of tenderness, and in the third study (27) botulinum toxin A was injected 5 cm distal to point of maximal tenderness at the lateral epicondyle. One RCT injected at a distance from the lateral epicondyle of 1/3 the total elbow to wrist distance (26). In 1 case series, botulinum toxin A was (25) injected 3 to 4 cm distal to tender lateral epicondyle and the other study did not specify the location of injection (24).

All of the RCTs studied used a VAS (0-100) scale for pain assessment. Three studies used a Jamar dynamometer and 1 used a Martin vigorimeter. These methods are highly correlated and could be considered equivalent (29). Only the study by Hayton and coworkers looked at quality of life (via SF-12) and showed no benefit in quality of life for botulinum toxin versus placebo (27).

Assessment of Risk of Bias

All 4 of the RCTs were well randomized. Three of the RCTs were double-blinded (13,14,26) and the other 1 was single-blinded toward the evaluator (27) (Table 1). Two of the RCTs performed an intention-to-treat analysis (14,26). One RCT (13) did not analyze the results from 1 subject of 130 according to intention-to-treat principles (129 analyzed as intention-to-treat). One RCT reported VAS pain scale in an unreliable manner (27).

Meta-Analysis

The primary analysis was the pooled results of the RCTs. At 3 months we found a pooled effect size for pain favoring botulinum toxin A (effect size −0.5, 95% CI −0.9, −0.1) (I^2 = 56%) (Fig. 2). The effect size for pain at 4 weeks from only 3 studies (13,14,26) also favored botulinum toxin (effect size −0.8, 95% CI −1.5 to −0.1). Only 1 study examined the 2-week time period (26) and showed a benefit for botulinum toxin at that time as well. One of the 4 had an individual effect size that was null (27) at 3 months. For grip strength, there was no statistically significant effect size despite a trend toward favoring botulinum toxin A. The pooled effect size was 0.2 (95% CI −0.2, 0.5).

Adverse Events

All RCTs collected information about adverse events. The most commonly reported events in the botulinum toxin groups were extensor weakness (transient in all cases), pain at the injection site, and paresthesia.

DISCUSSION

This systematic review and meta-analysis identified 10 studies evaluating botulinum for treatment of chronic lateral epicondylitis. The highest level evidence (the RCTs) shows a moderate benefit for botulinum toxin A injection for pain at 3 months in patients with chronic lateral epicondylitis that was resistant to other conventional therapies. Generally effect sizes of 0.2 are considered small; 0.5 are considered medium, and ≥0.8 are considered large

Table 2 Characteristics of the Participants In the RTCs

Study (Type)	TG (N)	TG Age	TG Sex[a]	CG (N)	CG Age	CG Sex[a]
Wong et al. (14) (RCT)	30	45.6 ± 9.1	25	30	44.2 ± 5.7	24
Hayton et al. (27) (RCT)	19	48 (35 to 71)[b]	19[b]	21	[b]	[b]
Placzek et al. (13) (RCT)	70	47.4 ± 8.7	37	62	46.9 ± 9.4	32
Espandar et al (26) (RCT)	24	43.3 ± 7.8	22	24	44.2 ± 7.7	22

TG, treatment group; CG, control group; NR, not reported.
[a]Number of females.
[b]Information provided for all study participants without dividing for treatment and control groups.

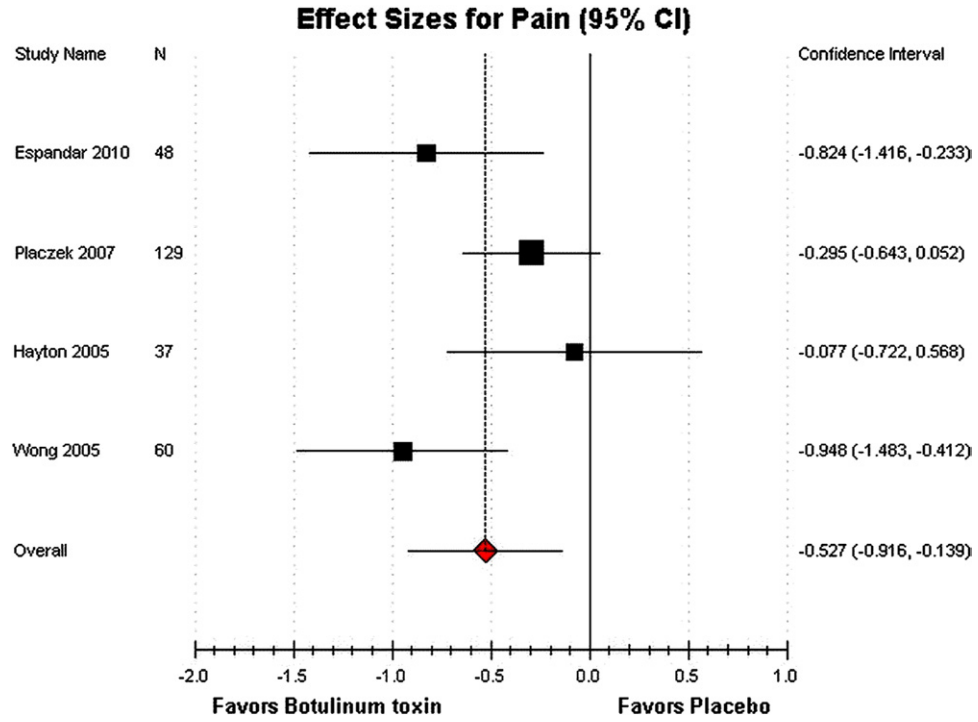

Figure 2 Effect sizes for pain. (Color version of figure is available online.)

(30). Given the lack of very effective treatments for chronic refractory lateral epicondylitis, this moderate effect is likely to be clinically meaningful to patients. The weaker evidence (case series) also supports the use of botulinum toxin in improving pain, but their interpretation is limited due to potential bias.

There was no statistical or clinical difference in grip strength at 3 months. Interpretation of grip strength data, however, might not be straightforward because the analysis included fewer trials and also there was a paucity of data among trials; consequently, influences of any gender and dominant hand effects on grip strength findings could not be fully evaluated.

Although botulinum toxin A has been used in various pain syndromes (10,11,31,32), its exact mechanism for relieving pain remains largely unknown (33-35). In lateral epicondylitis, it is believed that botulinum toxin A reversibly paralyzes the extensor muscles by temporarily blocking the neuromuscular end plate, thus preventing repetitive microtrauma of the tendinous fibers at their origin from the osseous lateral epicondyle, allowing them time to repair.

One of the possible sources of pain in lateral epicondylitis is the presence of active myofascial trigger points in forearm muscles (36). Several previous studies have shown that botulinum toxin is effective in the treatment of myofascial trigger points (31,37). Animal studies showed the suppressive effect of botulinum toxin A on endplate noise prevalence in the myofascial trigger point region (33). Although unclear, this is one of several potential mechanisms by which botulinum toxin improves pain in lateral epicondylitis. Because of the unknown mechanism of action, it is impossible to assign biologic plausibility to the location of injection, which did vary somewhat between studies.

This meta-analysis has several limitations. First, there were a small number of RCTs evaluating botulinum toxin A for lateral epicondylitis. We attempted to minimize publication bias by employing a broad search strategy independently by different reviewers and making author contacts wherever possible. We improved reliability of risk of bias assessment and data extraction as 2 reviewers performed procedures independently before consensus was obtained. The risk of bias of the studies in the meta-analysis was low; however, the only RCT that showed a null effect was of low quality and reported VAS pain scale in an unreliable manner, diminishing the quality of its results (27). Heterogeneity is a vulnerable point of all meta analyses. The heterogeneity of the studies included in the meta-analysis (I^2, 56%) was moderate. A final limitation is the time points available for analysis. The 3-month time point was consistent across studies. It is also frequently used as a goal of therapy clinically to improve pain within 3 months. It could be argued that a benefit of botulinum is early relief of pain. The only study to evaluate a 2-week time point supports that notion.

Adverse events were not uniformly reported in the studies, but we reported the data that were available. The use of botulinum toxin A for other indications adds some information about general safety. Long-term safety of botulinum toxin A for common therapeutic indications has been demonstrated in Cochrane Systematic Reviews and other meta-analyses; there were several adverse events, mild to moderate in severity, reported (38). There

were no reported occurrences of systemic botulism as a result of the injections in the reviewed literature. In addition, the high cost of botulinum toxin A also needs to be taken into consideration.

Botulinum toxin A should be considered as a viable treatment option in patients with chronic lateral epicondylitis who have failed conventional therapy. It is a minimally invasive procedure and can be performed in an outpatient setting. Further studies may be warranted to evaluate botulinum toxin A in individuals who have not had other therapies as well as to evaluate whether botulinum toxin A treatment affects return to work and sporting activities.

CONCLUSIONS

Present literature provides support for use of botulinum toxin A injections into the forearm extensor muscles (60 units Disport or equivalent) for the treatment of chronic treatment-resistant lateral epicondylitis.

ACKNOWLEDGMENTS

We are grateful to Usha M Sudireddy for her help in translating the German into English and to Chenchen Wang and Ling Li for translating the Chinese into English.

REFERENCES

1. Chiang HC, Ko YC, Chen SS, Yu HS, Wu TN, Chang PY. Prevalence of shoulder and upper-limb disorders among workers in the fish-processing industry. Scand J Work Environ Health 1993;19:126-31.
2. Shiri R, Viikari-Juntura E, Varonen H, Heliovaara M. Prevalence and determinants of lateral and medial epicondylitis: a population study. Am J Epidemiol 2006;164:1065-74.
3. Ranney D, Wells R, Moore A. Upper limb musculoskeletal disorders in highly repetitive industries: precise anatomical physical findings. Ergonomics 1995;38:1408-23.
4. Walker-Bone K, Palmer KT, Reading I, Coggon D, Cooper C. Prevalence and impact of musculoskeletal disorders of the upper limb in the general population. Arthritis Rheum 2004;51:642-51.
5. Hamilton PG. The prevalence of humeral epicondylitis: a survey in general practice. J R Coll Gen Pract 1986;36:464-5.
6. Verhaar JA. Tennis elbow. Anatomical, epidemiological and therapeutic aspects. Int Orthop 1994;18:263-7.
7. Struijs PA, Kerkhoffs GM, Assendelft WJ, Van Dijk CN. Conservative treatment of lateral epicondylitis: brace versus physical therapy or a combination of both-a randomized clinical trial. Am J Sports Med 2004;32:462-9.
8. Smidt N, van der Windt DA, Assendelft WJ, Deville 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;359:657-62.
9. Bisset L, Paungmali A, Vicenzino B, Beller E. A systematic review and meta-analysis of clinical trials on physical interventions for lateral epicondylalgia. Br J Sports Med 2005;39:411-22; discussion 411-22.
10. de Seze MP, de Seze M, Dehail P, Joseph PA, Lavignolle B, Barat M, et al. [Botulinum toxin A and musculoskeletal pain]. Ann Readapt Med Phys 2003;46:329-32.
11. Placzek R, Sohling M, Gessler M, Jerosch J. [Botulinum toxin A in orthopedic pain therapy]. Schmerz 2004;18:498-505.
12. Keizer SB, Rutten HP, Pilot P, Morre HH, v Os JJ, Verburg AD. Botulinum toxin injection versus surgical treatment for tennis elbow: a randomized pilot study. Clin Orthop Relat Res 2002; 125-31.
13. Placzek R, Drescher W, Deuretzbacher G, Hempfing A, Meiss AL. Treatment of chronic radial epicondylitis with botulinum toxin A. A double-blind, placebo-controlled, randomized multicenter study. J Bone Joint Surg Am 2007;89:255-60.
14. Wong SM, Hui AC, Tong PY, Poon DW, Yu E, Wong LK. Treatment of lateral epicondylitis with botulinum toxin: a randomized, double-blind, placebo-controlled trial. Ann Intern Med 2005;143:793-7.
15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med 2009;151:W65-94.
16. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm.
17. Cooper H, Hedges LV. The hand book of research synthesis. New York (NY): Russell Sage Foundation Publications; 1994.
18. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177-88.
19. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-60.
20. Wallace BC, Schmid CH, Lau J, Trikalinos TA. Meta-Analyst: software for meta-analysis of binary, continuous and diagnostic data. BMC Med Res Methodol 2009;9:80.
21. Guirao Cano L, Pleguezuelos Cobo E, Perez Mesquida ME, Sanz Cartagena P. Treatment of lateral epicondylitis with botulinus toxin. Rehabilitación 2004;38:196-8.
22. Morre HH, Keizer SB, van Os JJ. Treatment of chronic tennis elbow with botulinum toxin. Lancet 1997;349:1746.
23. Zhu Z, Chen WF, Lin L, Chen HX. [Botulinum toxin A for the treatment of refractory external humeral epicondylitis: a report of 58 cases]. Zhongguo Gu Shang 2008;21:465-6.
24. Oskarsson E, Piehl Aulin K, Gustafsson BE, Pettersson K. Improved intramuscular blood flow and normalized metabolism in lateral epicondylitis after botulinum toxin treatment. Scand J Med Sci Sports 2009;19:323-8.
25. Placzek R, Lindner MS, Deuretzbacher G, Meiss AL. [Therapy for chronic radial epicondylitis with botulinum toxin A]. Z Orthop Ihre Grenzgeb 2004;142:701-5.
26. Espandar R, Heidari P, Rasouli MR, Saadat S, Farzan M, Rostami M, et al. Use of anatomic measurement to guide injection of botulinum toxin for the management of chronic lateral epicondylitis: a randomized controlled trial. CMAJ 2010;182:768-73.
27. Hayton MJ, Santini AJ, Hughes PJ, Frostick SP, Trail IA, Stanley JK. Botulinum toxin injection in the treatment of tennis elbow. A double-blind, randomized, controlled, pilot study. J Bone Joint Surg Am 2005;87:503-7.
28. Bluthner M, Haugke C, Kalischewski P. Treatment of lateral epicondylitis elbow with botulinum toxin A—a first experience. Arch Pharmacol 2002;365(Suppl 2):R14-ABS-1147.
29. Desrosiers J, Hebert R, Bravo G, Dutil E. Comparison of the Jamar dynamometer and the Martin vigorimeter for grip strength measurements in a healthy elderly population. Scand J Rehabil Med 1995;27:137-43.
30. Cohen J. Statistical power analysis for the behavioral sciences, 2nd ed. Hillsdale (NJ): Lawrence Erlbaum Associates; 1988.
31. De Andres J, Cerda-Olmedo G, Valia JC, Monsalve V, Lopez A, Minguez A. Use of botulinum toxin in the treatment of chronic myofascial pain. Clin J Pain 2003;19:269-75.
32. Papapetropoulos S, Singer C. Botulinum toxin in movement disorders. Semin Neurol 2007;27:183-94.

33. Kuan TS, Chen JT, Chen SM, Chien CH, Hong CZ. Effect of botulinum toxin on endplate noise in myofascial trigger spots of rabbit skeletal muscle. Am J Phys Med Rehabil 2002;81:512-20; quiz 521-3.
34. Guyer BM. Mechanism of botulinum toxin in the relief of chronic pain. Curr Rev Pain 1999;3:427-31.
35. Voller B, Sycha T, Gustorff B, Schmetterer L, Lehr S, Eichler HG, et al. A randomized, double-blind, placebo controlled study on analgesic effects of botulinum toxin A. Neurology 2003;61:940-4.
36. Fernandez-Carnero J, Fernandez-de-las-Penas C, de la Llave-Rincon AI, Ge HY, Arendt-Nielsen L. Bilateral myofascial trigger points in the forearm muscles in patients with chronic unilateral lateral epicondylalgia: a blinded, controlled study. Clin J Pain 2008;24:802-7.
37. Kamanli A, Kaya A, Ardicoglu O, Ozgocmen S, Zengin FO, Bayik Y. Comparison of lidocaine injection, botulinum toxin injection, and dry needling to trigger points in myofascial pain syndrome. Rheumatol Int 2005;25:604-11.
38. Naumann M, Albanese A, Heinen F, Molenaers G, Relja M. Safety and efficacy of botulinum toxin type A following long-term use. Eur J Neurol 2006;13(Suppl 4):35-40.