BMJ open

Treating lateral epicondylitis with corticosteroid injections or non-electrotherapeutical physiotherapy: a systematic review

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-003564
Article Type:	Research
Date Submitted by the Author:	09-Jul-2013
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Primary Subject Heading:	Sports and exercise medicine
Secondary Subject Heading:	General practice / Family practice
Keywords:	SPORTS MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, Elbow & shoulder < ORTHOPAEDIC & TRAUMA SURGERY

Abstract

Objectives

To evaluate the efficacy of corticosteroid injection and non-electrotherapeutic physiotherapy, commonly used treatments for lateral epicondylitis, but for which the scientific evidence remains uncertain.

Design

Systematic review.

Setting

n/a

Participants

We searched five databases in September 2012 for randomized, controlled studies with a minimum quality rating. Of 640 studies retrieved, eleven were included, representing 1161 patients of both sexes and all ages.

Interventions

Corticosteroid injection and non-electrotherapeutic physiotherapy.

Outcome measures

Relative risk (RR) or standardised mean difference (SMD) for overall improvement, pain and grip strength at 4 to 12, 26 and 52 weeks follow-up.

Results

Corticosteroid injection gave a short-term reduction in pain vs no intervention or NSAIDs (SMD -1.43, 95% CI -1.64 to -1.23). At intermediate follow-up, we found an increase in pain

(SMD 0.32, 95% CI 0.13 to 0.51), reduction in grip-strength (SMD -0.48, 95% CI -0.73 to -0.24), and negative effect on overall improvement effect (RR 0.66 (0.53 to 0.81). For corticosteroid injection vs lidocaine injection, evidence was conflicting. At long-term follow up, there was no difference on overall improvement and grip strength, with conflicting evidence for pain. Manipulation and exercise vs no intervention showed beneficial effect at short-term follow-up (overall improvement RR 2.75, 95% CI 1.30 to 5.82), but no significant difference at intermediate or long-term. We found moderate evidence for a short- and long-term effect of eccentric exercise and stretching vs no intervention. For exercise vs no intervention and eccentric or concentric exercise and stretching vs stretching alone, we found moderate evidence of no short-term effect.

Conclusions

Corticosteroid injections have a short-term beneficial effect on lateral epicondylitis, but a negative effect at intermediate term. Evidence on long-term effect is conflicting. Manipulation and exercise and exercise and stretching have a short-term effect, the latter also a long-term effect.

Trial registration

None.

Article summary

Article focus

- What is the current evidence for the effect of treating lateral epicondylitis with corticosteroid injection or non-electrotherapeutic physiotherapy?

Key Messages

- Corticosteroid injections have a short-term beneficial effect on lateral epicondylitis, but a negative effect at intermediate term. Evidence on long-term effect is conflicting.
- There is evidence for a short-term effect of manipulation and exercise and exercise and stretching, for the latter also on long-term.

Strengths and limitations of this review

- We found overall few good quality studies on these treatments, making a meta-analysis possible only for a few studies and outcomes.

Introduction

Lateral epicondylitis of the elbow is a frequently encountered complaint in general practice with an incidence of 4 - 7 per 1000 per year [1-3]. It is characterised by pain and tenderness over the lateral humeral epicondyle and pain on resisted dorsiflexion and radial deviation of the wrist. It is usually a self-limiting condition, often resolving in 6 to 12 months regardless of treatment, but complaints may last up to 2 years or longer [4]. Due to considerable pain and discomfort, many patients need time off from work.

Most authors attribute the condition to a lesion in the short radial extensor muscle [1, 5]. A recent study has found evidence of reduced hyperaemia measured with spectral and colour Doppler in lateral epicondylitis treated with corticosteroid injection, suggesting evidence of an inflammatory component [6]. Others, finding little evidence of inflammation have proposed the term "lateral epicondylalgia" for the condition [7].

Most patients with lateral epicondylitis are treated in general practice, and although a large number of treatments are in use, there is no consensus on which treatments are most effective. The Cochrane Library has reviewed several treatments. For topical NSAIDs and NSAIDs taken orally, the conclusion is that both have a short term effect [8]. For extracorporeal shockwave therapy, a review of nine studies including 1000 patients found this treatment to have no effect [9]. For acupuncture [10], deep friction massage [11], orthosis [12] and surgery [13] the reviews were inconclusive due to few and methodologically weak studies.

Four review articles have been published on the effect of corticosteroid injections [14-17]. They found a short-term effect of corticosteroid injection, but no proven long-term effect, and one review found evidence of a negative long-term effect [15]. However, some of the reviews included non-controlled studies [14, 16] and non-randomised studies [16]. In one

review [15], four of 12 included studies had no control group and one was a small pilot study with short follow up. Based on this, we find the evidence in published reviews on the long-term effect of corticosteroid injections to be conflicting.

Five reviews of physiotherapeutic interventions show that there are few published studies on the effect of non-electrotherapeutic treatment, and many have methodological weaknesses [16, 18-21]. Bisset et al. [18] found evidence that manipulation and exercise had a short term effect. Four other reviews [16, 19-21] found short-term effects of mobilisation, manipulation and exercise. Three of these reviews included non-randomised or non-controlled studies [16, 19, 21]. Most previous systematic reviews have included electrotherapeutic physiotherapy such as ultrasound and extra-corporeal shockwave [14, 16, 20, 21].

Since there is no established, well-documented treatment to which new treatments can be compared, the use of a control group is important. The natural course of the condition, where most patients eventually recover regardless of intervention, makes this even more necessary. In a comparison of two different treatments, any effect found may only reflect this natural course of recovery unless the treatments prove better than a control group with no treatment.

It has been shown that systematic reviews which include studies with low scores on internal validity may over-estimate effect sizes, thus introducing a potential bias to the review [22]. There may also be a problem using rating scales with heterogeneous criteria, including i.e. criteria related to external validity, interpretation or ethical issues [22, 23].

To address these issues, a new systematic review on non-electrotherapeutic physiotherapy and corticosteroid injection seemed warranted. We wanted to include only randomised studies with a control group with no treatment or studies in which the groups only differed in regards to the investigated treatment. An established quality rating scale would be

used. We also wanted to review the most current evidence on the efficacy of corticosteroid injection, since previous reviews have differing conclusions on long-term effect.

Objective

The aim of this review was to assess the current evidence for the efficacy of corticosteroid injection and non-electrotherapeutical physiotherapy compared with control in patients with tennis elbow.

Methods

We followed the recommendations of the Cochrane Collaboration [24] and the PRISMA Group [25] in the search and report of this systematic review.

Study selection

We used the following inclusion criteria:

Study type

Randomized, controlled trials assessing treatments for lateral epicondylitis or tennis elbow were eligible for inclusion. The studies had to have at least one treatment group and one control group. We defined a control group as a group receiving no treatment (a wait-and-see approach), common treatments with expected or known moderate effect (advice, rest, NSAIDs, pain-killers) or the same treatment as the experimental group with the exception of the investigated treatment.

Participants

All age groups with a clinical diagnosis of lateral epicondylitis were included without restriction on gender.

Treatments

We searched for studies investigating or comparing the efficacy of one of the following treatments: corticosteroid injection, non-electrotherapeutic physiotherapy including stretching, mobilisation, manipulation, massage, exercise or home training. Studies on splinting, ultrasound, shock wave and other electrotherapeutic modalities were excluded.

Outcome measures and follow up

At least one validated, patient-centred outcome was necessary. This could include outcomes important to the patient such as pain, range of movement, grip strength, work status and relevant functional questionnaires. We included only studies done in a clinical setting with at least four-week follow-up of treatment effect.

Study quality assessment

We used the 11-item PEDro scale to assess the quality of the studies included in the review. This rating system closely resembles the Cochrane Collaboration Scoring system [24] and is based on the Delphi list, developed for quality assessment of randomised controlled trials by Verhagen et al. [26]. It has been used in several previously published reviews [15, 18, 19]. The PEDro scale assesses the internal and external validity of a study by addressing the issues of eligibility criteria, randomisation, allocation, blinding, statistics and data reporting. The reliability of this scale has been confirmed by Maher et al in 2003 [27]. The maximum score is 10, since item number one on the scale (specified eligibility criteria) is not counted.

A minimum score of 5 out of 10 points (50%) was chosen to be necessary for inclusion in the review, as inclusion of lower quality studies in a systematic review may over-estimate the treatment effect of interventions [28]. Ten studies were independently assessed

by two researchers (MO, ØH) [29-38] and three studies were rated by both researchers together [39-41]. The final decision on PEDro score was reached by consensus.

Search methods for identification of studies

Electronic searches

From October 2009 to January 2010, we searched the following databases for publications: Medline (Ovid and PubMed), EVSCO/Cinahl, Embase, Allied and Complimentary Medicine, The Physiotherapy Evidence Database (PEDro) and the Cochrane RCT register. The searches within each database were done without restrictions on dates or languages. We used free text, not MESH terms, in these searches, and the key terms used were ”tennis elbow”, ”lateral epicondylitis”, epicondylalgia, elbow, randomised, randomized, injection, corticosteroid, and physiotherapy. The Boolean operator AND was used to link diagnostic terms and treatment where applicable. An additional search was done in September 2012 to identify any recently published studies.

Searching other resources

Further search was done in the reference list of articles initially considered for review.

Selection of studies

The searches resulted in a number of studies potentially eligible for inclusion. Titles and abstracts were then read by two researchers independently (MO, ØH) and potential studies were selected based on the inclusion criteria. The final decision on inclusion was made by consensus from reading the full-text documents.

Data extraction and statistical analysis

The included studies were read in full text and assessed by two independent researchers (MO, ØH). One article, published in Italian, was translated by a professional bureau [41]. A

standardized set of data was extracted from each selected study and recorded using standardized forms. We calculated statistics using the statistical computing language R (www.r-project.org, The R Foundation for Statistical Computing, Vienna, Austria). We reported the results of the outcome measures for three different timings of follow-up, defined as short-term (four to 12 weeks after randomisation), intermediate term (six months after randomisation) and long-term (more than six months after randomisation). For dichotomous data, we calculated relative risk (RR) and 95% confidence intervals (CI) with the R-project library "epi.R", for continuous data the standardised mean difference (SMD) and 95% CI with the R-project library "compute.es". We pooled estimates when we found sufficient clinical and statistical homogeneity between trials using the I^2 statistic, defined as I^2 less than 65% [42].

Some studies did not report the mean, standard deviation or number of samples, which were necessary to calculate SMD. Additional calculations were then required. For Coombes [38], the median and the interquartile range (IQR) were given. We set the median as the mean value and the standard deviation was given by IQR/1.35 under the assumption of normal distribution. For Newcomer [33], the standard deviation was calculated by t-statistics obtained by the p-value and degrees of freedom. For Price [34], the t-statistics was obtained by the degrees of freedom and 95% probability. The standard deviation was estimated by the t-statistics, the mean value and upper/lower confidence intervals.

For overall improvement, a RR larger than 1 favoured treatment, and was statistically significant if the CI excluded 1. We defined the effect as large for values larger than 2 or less than 0.5, medium between 0.5 and 0.8 and between 1.25 and 2 and small for values between 0.8 and 1.0 and between 1.0 and 1.25.

For continuous data, a positive or negative SMD favoured treatment depending on the outcome measures, ie. for pain a negative SMD favoured treatment and for grip strength a

positive SMD favoured treatment. SMD was statistically significant if the CI excluded zero. We defined the effect as large for SMD more than 0.8, medium between 0.5 and 0.8 and small for values less than 0.5. For outcomes that could not be pooled, we graded the strength of the scientific evidence as strong (consistent findings in several high-quality randomised controlled studies), moderate (one high-quality randomised controlled study), conflicting (inconsistent finding between many studies) or no evidence [43].

Inter-rater reliability

The inter-rater reliability for the individual PEDro scores was assessed by calculating the intra-class correlation coefficient [44]. The R-project library "psych" was used for this calculation. A substantial inter-rater reliability was found (intra-class correlation coefficient 0.69 (0.15-0.91), $p<0.01$).

Results

The search retrieved an initial 839 hits, representing 640 individual articles. The further selection process is outlined in Figure 1. 623 articles were excluded based on title and abstract in a preliminary review. 17 articles [29-37, 39, 41, 45-50] were then assessed using the full-text documents. Three were found not to be randomised controlled trials [45-47], two had a PEDro quality rating below 50% (Table 2) [37, 39] and three had a follow-up shorter than four weeks [48-50]. The additional search done in september 2012 retrieved two possible studies [40, 51], one of which was excluded for not having a control group [51]. A recently published study was also assessed [38] and a total of 11 studies were included in the final review [29-36, 38, 40, 41].

Included studies

The characteristics and details of each study are given in Table 1. The included studies represented a total population of 1161 patients. Several studies had more than one treatment

group, so the 11 included studies investigated 15 treatment groups relevant for this review. For the statistical analysis, one study which used two different corticosteroids, was treated as two studies [34].

The mean age of patients varied from 41 to 51 years and the female percentages varied from 35 to 63. There were large differences in duration of complaints at baseline between studies. Most had a duration of several weeks to months and only one stated a short duration [33]. Eight studies had control groups with no active treatment [29-31, 34-36, 38, 40], e.g. a wait-and-see group or NSAIDs. Two of these used lidocaine as a placebo injection [31, 34]. In the three other studies, the control and treatment groups both received similar active treatments, with the intervention group in addition receiving the treatment to be investigated [32, 33, 41] .

Eight studies investigated corticosteroid injections, representing 925 patients [29-31, 33-36, 38]. Five different corticosteroids were used, with different dosages and injection techniques. The control groups received no active treatment in seven of the eight studies, in one study both the control and treatment group received additional exercise treatment [33]. Seven of the studies had a long-time follow up of 24 weeks or more [29-31, 33-35, 38].

There were few studies covering non-electrotherapeutic physiotherapy. We found five studies which could be included, representing 600 patients [29, 32, 38, 40, 41]. The treatment modalities investigated were manipulation and exercise [29, 38], concentric or eccentric exercises [32], exercise [40] and eccentric exercises with stretching [41]. Three studies had a control group with no active treatment [29, 38, 40], the other two had control groups that received stretching and orthosis respectively. Three studies [29, 38, 41] had a follow up of 24 weeks or more.

The most frequently used outcome measures were assessment of pain and grip strength. Six studies measured pain free grip strength with handheld dynamometers [29-33,

35]. Eight studies used a number of different questionnaires covering pain, function and disability [29-33, 35, 38, 40]. Nine studies assessed pain on a visual analogue scale or Likert-scale [29-34, 36, 38, 40], and six studies rated patient's assessment of improvement on graded scales [29, 30, 35, 36, 38, 41].

Risk of bias in included studies

We addressed the issues of the quality of the included studies and completeness of reported data by rating them with the PEDro scale (Table 2). Most studies used a computerized randomisation schedule, and seven of the eleven studies used concealed allocation [29-31, 35, 38, 40, 41]. Baseline comparison was done in all studies, the dropout rate was below 15% in ten studies [29, 30, 32-36, 38, 40, 41] and intention to treat analysis was stated in all studies. There was between-group analysis of at least one outcome measure in all the studies, and both point-measures and variations of outcome measures were reported in all studies.

The use of blinding was more diverse among the studies. Blinding the subject for treatment is difficult for physiotherapeutic treatments, but the use of blinded assessors reduces the risk of bias. None of the studies on physiotherapy in our review had blinded subjects or therapists, but two used blinded assessors [29, 38]. This might give biased results in the studies covering physiotherapeutic treatments.

For the eight studies on corticosteroid injection, the number using blinding was larger. There was blinding of subjects in four studies [31, 33, 34, 38], of the treating doctor in two [31, 33] and of assessors in six studies [29-31, 34, 35, 38].

In several studies the control group received some form of treatment (although similar to the treatment group) [32-34, 36, 41]. In these studies, synergistic effects between the treatments cannot be ruled out. This makes the results more difficult to interpret. Two studies had a short follow up of four and six weeks [32, 36], which for a condition usually lasting

several months, reduces the clinical implication of the results. Difference in duration of complaints at baseline also complicates comparison between studies.

Effects of interventions

Corticosteroid injection

The efficacy of corticosteroid injection for treating lateral epicondylitis was investigated in eight studies (Table 3 and Figure 2 [52]). For short-term follow up, heterogeneity between studies made pooling of outcomes only possible for pain. For corticosteroid injection vs no intervention or NSAIDs, we found strong evidence for a beneficial effect on overall improvement and a large positive effect on pain [29, 30, 35, 36, 38]. For grip strength, we found moderate evidence for a negative effect [35]. For corticosteroid injection vs lidocaine injection, evidence was conflicting for effect on pain, with two studies showing a large positive effect (Price et al. using hydrocortisone and triamcinolone) [34] and one showing no significant difference [31]. For maximum grip strength, the evidence was also conflicting, with one study showing a large postitive effect of treatment (Price et al. using triamcinolone)[34], and two studies showing no statistical difference (Lindenhovius, Price et al. using hydrocortisone) [31, 34]. For corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found moderate evidence for no significant difference on pain and grip strength [33].

At intermediate follow-up, we found sufficient homogeneity to poole estimates for overall improvement [29, 30, 38] and pain [29, 30, 35, 38] for corticosteroid injection vs. no intervention or NSAIDs. For overall improvement this showed a medium negative effect and for pain a small negative effect. For maximum grip strength, pooling of corticosteroid injection vs no intervention, NSAIDS and lidocaine showed a small negative effect [31, 34, 35]. For corticosteroid injection vs lidocaine injection, pooling of estimates was not possible due to heterogeneity. For pain, two studies showed a large negative effect (Price et al. using

hydrocortisone and triamcinolone)[34], and one study showed no significant difference [31], thus the evidence was conflicting. For grip strength, the evidence was also conflicting, with the same two studies showing a large negative effect [34] and one showing no significant difference [31]. For corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found moderate evidence of no significant effect on pain [33].

At long-term follow-up, pooled estimates of overall improvement showed no difference in effect of corticosteroid injection vs no intervention or NSAIDs [29, 30, 35, 38]. For pain, heterogeneity prevented pooling and we found the evidence conflicting with one study showing a large negative effect [30], and three others showing no significant difference in effect [29, 35, 38]. For grip strength, we found moderate evidence of no significant difference [35]. For corticosteroid injection vs lidocaine injection and corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found no data on long-term effect.

Physiotherapy

We included five studies (n=600) investigating non-electrotherapeutical physiotherapy, representing five different treatment modalities (Table 4 and Figure 3 [52]).

Two studies investigated the efficacy of manipulation and exercise vs. no intervention [29, 38]. At short-term, pooled estimates showed a large positive effect on overall improvement. For pain, pooling was not possible due to heterogeneity. We found strong evidence for a beneficial effect, for pain free grip strength we found moderate evidence for a beneficial effect. At intermediate-term, pooled estimates showed no difference between treatment and control for neither pain nor overall improvement. There was moderate evidence for no difference in pain free grip strength. At long-term, pooled estimates again showed no difference between treatment and control for either pain or improvement and we found moderate evidence for no difference in pain free grip strength.

The efficacy of exercise vs no intervention was investigated in one study [40]. We found moderate evidence for no short-term difference in effect for outcomes on pain and DASH-score. There was no data on intermediate- or long-term effect.

For eccentric exercise and stretching vs stretching, investigated in one study [32], we found moderate evidence for no short-term treatment effect for outcomes on pain, pain-free grip strength and DASH-score. There was no data on intermediate- or long-term effect.

The same study also investigated the efficacy of concentric exercise and stretching vs stretching. We found moderate evidence for no short-term treatment effect for outcomes on pain, pain-free grip strength and DASH-score. There was no data on intermediate- or long-term effect.

Eccentric exercise and stretching vs no intervention was investigated in one study [41]. We found moderate evidence for a positive effect on pain and grip strength at short-term follow up. There was no data on efficacy at intermediate follow-up, but at long-term, we found moderate evidence of a positive effect on overall improvement, pain and grip strength.

Discussion

Summary of main results

This review found overall evidence for a short-term beneficial effect of corticosteroid injection. At intermediate follow-up, the evidence showed an overall negative effect. For corticosteroid injection vs lidocaine injection, we found the evidence to be conflicting. At long-term follow up, the evidence suggest no difference in effect on overall improvement and grip strength, but the evidence was conflicting for pain. For manipulation and exercise vs no intervention, we found an overall beneficial effect at short term, but no significant difference at intermediate or long-term follow-up. The evidence on exercise vs no intervention showed no differences at short-term follow up. For eccentric exercise and stretching vs stretching

alone, the evidence showed no short-term difference in effect. The same was found for concentric exercise and stretching vs stretching. The evidence on eccentric exercise and stretching vs no intervention showed a beneficial effect at short-term and long-term, while there was no data on intermediate follow-up.

For treating lateral epicondylitis, this review showed evidence for a short-term benefit of corticosteroid injection and manipulation with exercise. Eccentric exercise and stretching showed beneficial effect both at short- and long-term follow-up.

Overall completeness and quality of the evidence

There is a paucity of well-designed studies for determining the effect of non-electrotherapeutic physiotherapy. The conclusions on the effect of these treatments are therefore limited. A comparison and review of several individual studies was only possible for one treatment modality, manipulation and exercise vs no intervention (Table 4).

We included eight studies treating a total of 925 patients with corticosteroid injections in our review. The conclusions for this treatment are more solid due to the larger number of studies, seven of which had long-term follow up. Due to differences in type of corticosteroids used, treatment regimes and outcome measures in the included studies, pooling of outcome measures was difficult. We found statistical heterogeneity for most outcomes, and pooling was only possible for a few of the outcomes and follow-ups. The long-term effect of corticosteroid injection showed conflicting results in the included studies. The large differences across the studies in duration of complaints at baseline, corticosteroids used in different dosages, and control group treatments may explain this.

The difference in duration of complaints at baseline complicates the interpretation and comparison of the results, since there might be different effects of the treatments on an epicondylitis of recent onset compared to one that has lasted several months. This is also reflected by Cook [53] who considered tendinopathy as a continuum with three stages and

different characteristics and presumably treatments for each stage. Haahr [54] found that high physical strain at work, work with manual tasks, high perceived stress at baseline and a high level of pain and dysfunction seem to predict an unfavourable outcome after one year. Thus any differences in baseline characteristic for these parameters might possibly influence between-group differences of outcome.

Potential biases in the review process

The search process, selection of search terms and possible errors in reading and assessing the large number of articles represent a possible bias. Although we have searched several databases with a number of search terms, we may have missed some published studies. To reduce the risk of bias in the inclusion process, we used two reviewers who independently screened articles.

Our choice of inclusion criteria, especially the type of control or comparison treatment and the use of a cut-off quality score (PEDro), has important implications for the conclusions that can be drawn from this review. The efficacy of the treatments are here only compared with a control (no treatment) or to an underlying treatment that is common to both intervention groups, so no conclusion can be drawn on which of two different treatments is best.

To address the issue of publication bias, we searched two clinical trial registries: ClinicalTrial.gov (US National Institutes of Health) and Current Clinical Trials. We found no completed, unpublished studies on corticosteroid injection. Two completed studies on non-electrotherapeutic physiotherapy were found. One from The United Kingdom completed in 2008 on manipulation with movement and one from Sweden completed in 2009 on eccentric training. We have found no published articles from these studies. Unpublished studies are not indexed in PubMed or other databases and older studies may have been conducted without

registration in a clinical trial registry, making it difficult to make an overall assessment of publication bias.

Agreements and disagreements with other reviews

Our findings agree with earlier reviews [14, 16, 17, 55]. We found consistent evidence of a beneficial short-term effect of corticosteroid injections, but evidence on the long-term effect is still conflicting. Coombes et al. [15] found in their review that corticosteroid injections have a worse outcome in the long term than most conservative interventions for tendinopathies of different locations. The included studies in our review did not allow for a similar strong conclusion on the long-term effect of corticosteroid injections. For non-electrotherapeutical physiotherapy, we agree with earlier reviews [14, 16, 18, 19, 21] that there is moderate evidence of a short-term effect of manipulation and exercise. Our review strengthens this conclusion with the inclusion of a recently published study [40]. In addition, we found moderate evidence of both short- and long-term beneficial effect of eccentric exercise and stretching.

Authors' conclusions

Implications for practice

For lateral epicondylitis, this review found support for the use of corticosteroid injection for a short-term effect. The improvement in outcome measures was in our view of such a degree that it is clinically significant (Table 3, Figure 2). The negative intermediate effect and conflicting long-term effect make the treatment decision more difficult. Lateral epicondylitis is a self-limiting complaint that usually resolves in 6 to 12 months regardless of treatment. Thus, one could be tempted to refrain from active intervention. However, the effect of corticosteroid injection in the short term would be a strong argument for its use for many patients, even at the risk of a relapse. This could improve the ability to be at work or other

physical activities. As long as the evidence for an inferior long-term effect is conflicting, we find it difficult to advice against the use of this treatment if it can reduce the patient's symptoms for some of the time the condition takes to heal. These issues should be discussed with the patient as part of deciding the best treatment for each patient. We found some support for recommending the use of manipulation with exercise and eccentric exercise with stretching.

Implications for research

Further randomised, controlled trials are needed to investigate the intermediate and long-term efficacy of corticosteroid injection. A meta-analysis with individual patient data from earlier studies might give more answers to the question on long-term effect. The effect of different corticosteroids, dosages and injection techniques need to be investigated.

For non-electrotherapeutical physiotherapy, more studies with a randomised, controlled design are needed. Blinding, for example by using a blinded assessor, should be apllied wherever possible. The promising results on manipulation with exercise and eccentric exercise with stretching needs further investigating.

Future studies should differentiate between acute and chronic complaints. Baseline levels of perceived pain, stress levels, handedness and presence of physical stress at work should be recorded. Standardization in the usage of outcome measures will enable data pooling and meta-analyses in future reviews. Studies investigating the combined effect of physiotherapy and corticosteroid injection treatments would also be useful. Most patients with acute lateral epicondylitis are treated in a general practice setting, and future research should be performed in such a setting.

Acknowledgements

Morten Olaussen and Oeystein Holmedal designed the study, performed the searches, read articles, decided which articles to include, performed the data extractions, interpreted the findings and wrote the main manuscript. Morten Lindbaek designed the study, decided which articles to include, interpreted the findings and revised the manuscript. Soeren Brage decided which articles to include, interpreted the findings and revised the manuscript. Hiroko Solvang did the statistical calculations and analysis, interpreted the findings and revised the manuscript.

Competing interests

The authors declare that they have no competing interests.

Funding

Our work was funded by The Fund for General Practice Research, The Norwegian Medical Association, Oslo, Norway.

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FIGURES AND TABLES

uploaded as web only data:

Table 1: Demographics, treatments and outcome measures in the ten included studies

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Table 4: Effect size of treatment effects for non-electrotherapeutic physiotherapy

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Figure 3: Forest-plot of effect sizes for non-electrotherapeutic physiotherapy

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	in title
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	in abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	12
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8-10

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	17
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	na
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10-12, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13-15, table 3,4, figure 2,3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13-15. table 3,4, figure 2,3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10,12,17,
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	na
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16-18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18-19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Figure 1: Outline of the selection process

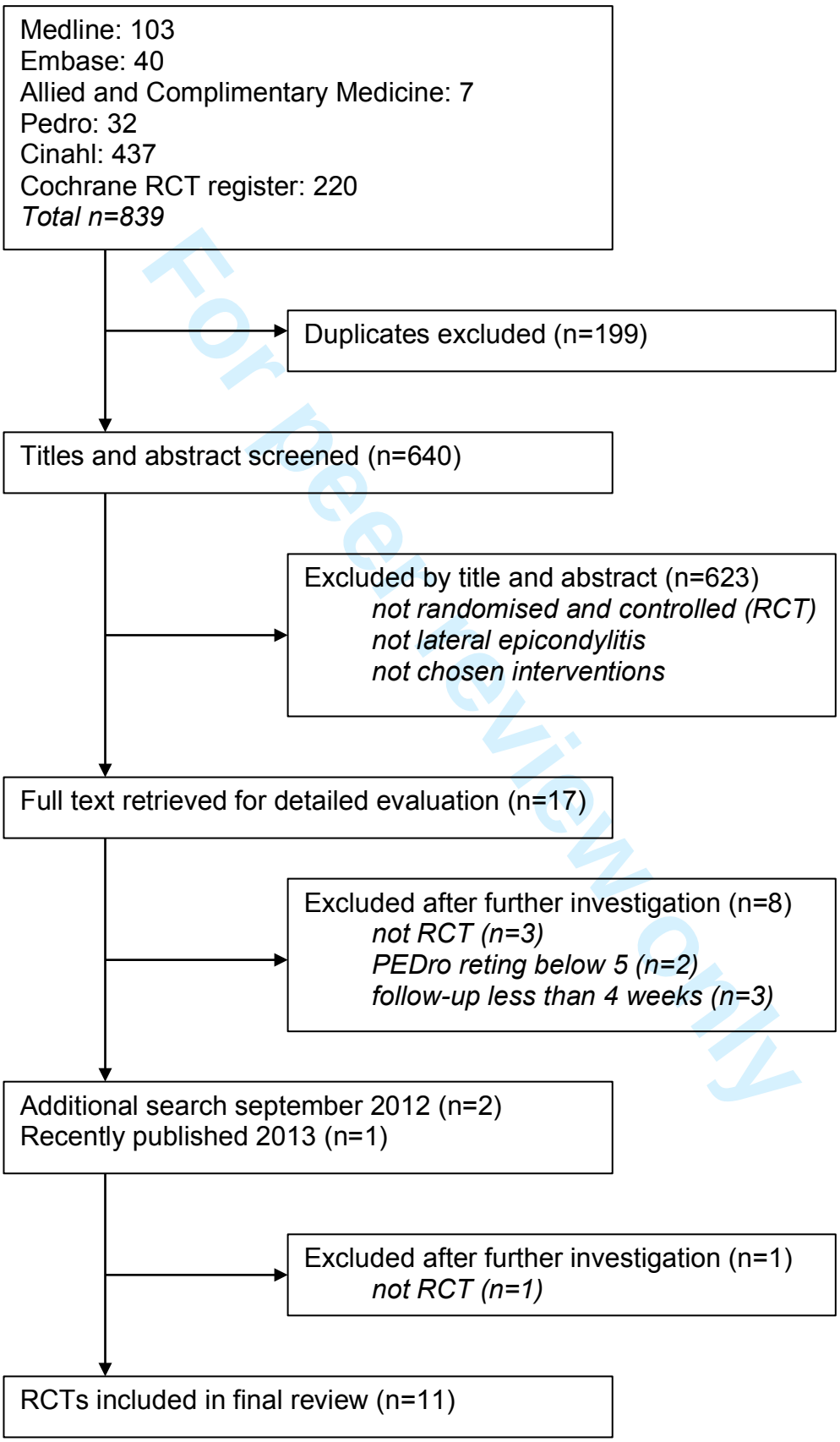
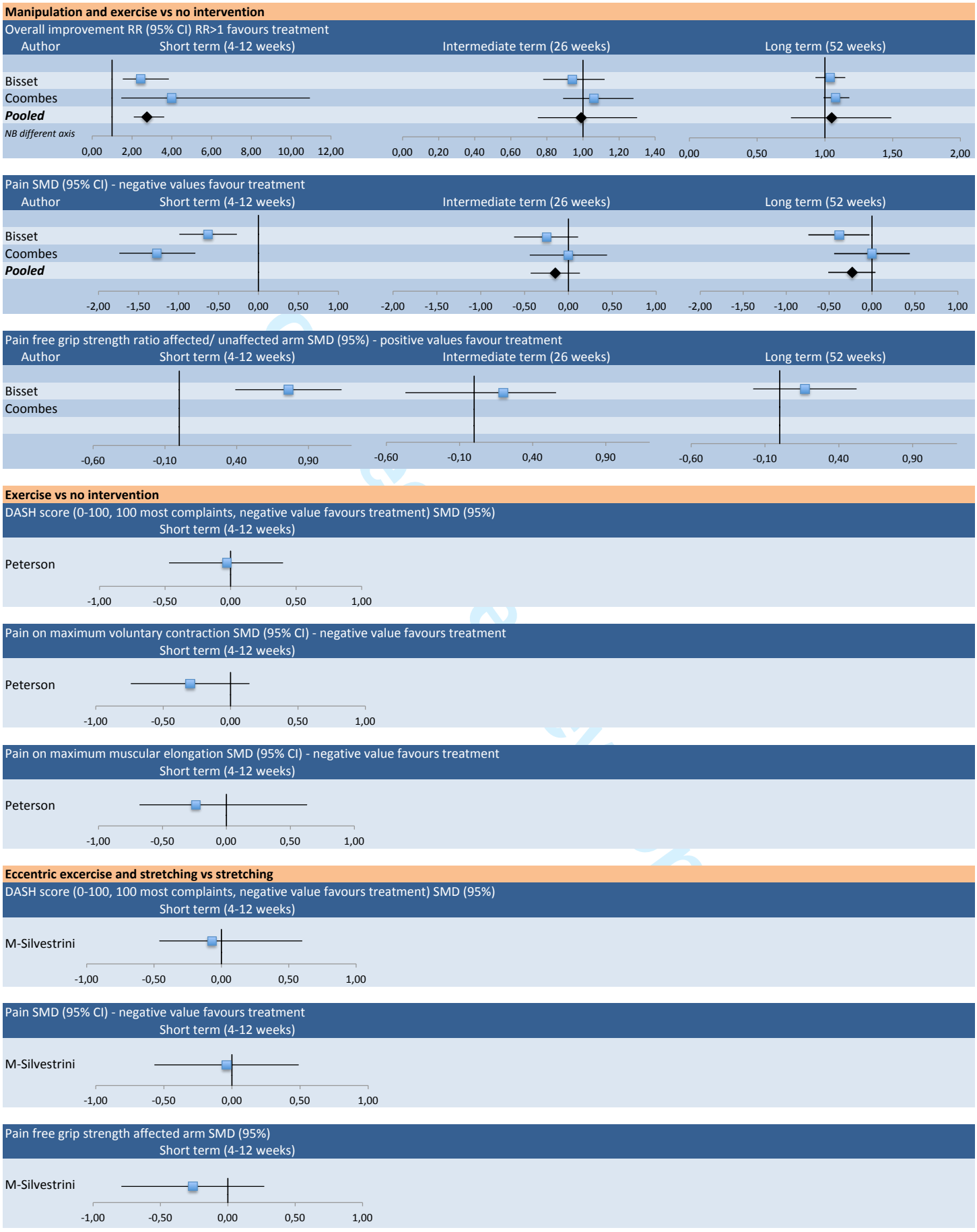


Figure 2. Forest-plot of effect sizes for corticosteroid injection

RR: relative risk
SMD: standardised mean difference
1: Corticosteroid injection (CSI) vs no intervention or NSAIDs
2: CSI vs lidocaine injection
3: CSI, excercise and stretching vs excersise and stretching. The values for Newcomer are given as change in pain and change in pain free grip strength.

Price 1: hydrocortisone vs lidocaine
Price 2: triamcinolone vs lidocaine

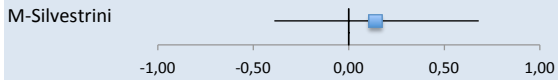
Figure 3. Forest-plot of effect sizes for non-electrotherapeutic physiotherapy



Concentric excercise and stretching vs stretching

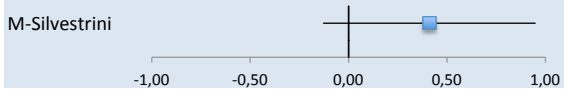
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95%)

Short term (4-12 weeks)



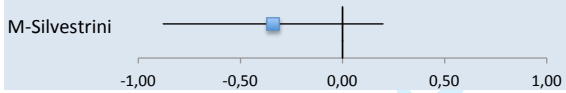
Pain SMD (95% CI) - negative value favours treatment

Short term (4-12 weeks)



Pain free grip strength affected arm SMD (95%)

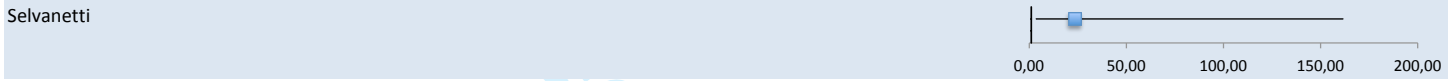
Short term (4-12 weeks)



Eccentric excercise and stretching vs no intervention (sham ultrasound, elbow support)

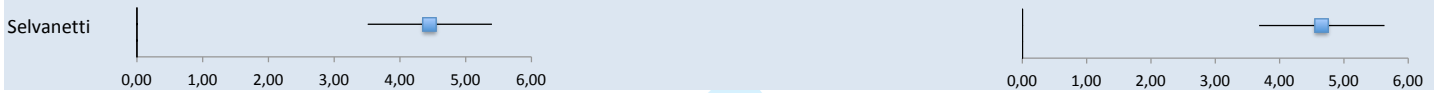
Improvement/success RR (95% CI) - RR>1 favours treatment

Short term (4-12 weeks) | Intermediate term (26 weeks) | Long term (52 weeks)



Pain on Ko-scale (larger value means less pain) SMD (95% CI)

Short term (4-12 weeks) | Intermediate term (26 weeks) | Long term (52 weeks)



Grip strength on Ko-scale (larger value means greater strength) SMD (95%)

Short term (4-12 weeks) | Intermediate term (26 weeks) | Long term (52 weeks)

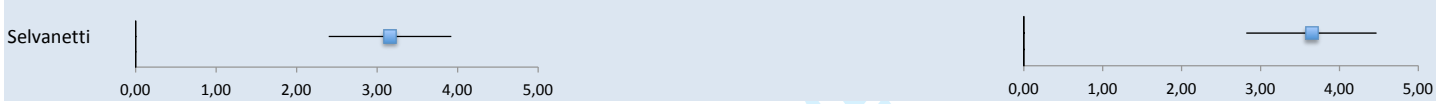


Table 1: Demographics, treatments and outcome measures in the eleven included studies

Study and year *setting and sample size*	Women *(percentages)*	Age *(mean if not otherwise stated)*	Duration of complaints *(weeks)*	Treatment groups	Control group	Outcome measures *(excerpts)*	Follow up *(weeks)*
Bisset et al. 2006 *Outpatient clinic* *n=198*	35	47,6 (SD 7.8)	22 (median) (IQR: 12-42)	1: 10 mg triamcinolone and 1 ml lidocaine against the most painful point repeated after 2weeks 2: Elbow manipulation (manipulation with mowement) and excercise 8 sessions of 30 minutes duration during a 6 week period and home exercise	Information, wait-and-see	Improvement on 6-point Likert-scale Pain free grip strength (PFGS) Assessed severity on VAS-scale (Visual Analogue Scale) Pain on VAS Pain free function questionnaire	52
Coombes et al. 2013 *Community setting* *n=165*	38	49.7 (SD 8.1)	16 (median) (IQR 10-26)	1: One injection of 1 ml triamcinolone 10 ml/ml and 1 ml lignocaine 1% against site of greatest palpable tenderness at the common extensor origin 2: Elbow manipulation (manipulation with mowement) and excercise 8 sessions of 30 minutes duration during a 8 week period and home exercise *3: One injection of triamcinolone followed by 8 sessions of elbow manipulation and excersie, home excercise for 8 weeks (not considered in this review)*	Placebo injection 0.5 ml 0.9 % isotonic saline	Improvement on 6-point Likert-scale One year recurrence Pain on VAS PRTEE questionnaire †† EuroQol-EQ-5D quality of life score	52
Hay et al. 1999 *General practice* *n=164*	Group 1: 41 (Group 2: 53) Control: 48	Age ≥ 45: (percentages) Group 1: 70 (Group 2: 68) Control: 38	9 (mean) Percentage with pain >3 months: Group 1: 36 (Group 2: 25) Control: 31	1: One injection of methylprednisolone 20 mg and 0.5 ml 1% lignocaine towards tender spot *2: Naproxen po 500 mg bid for 2 weeks (not considered in this review)*	Placebo tablets	Improvement on 5-point Likert-scale Pain on 10-point Likert-scale Function on 10-point Likert-scale Main complaint on 10-point Likert-scale Disability questionnaire PFGS	52
Price et al. 1991 *Outpatient clinic* *n=88*	Group 1: 48 Group 2: 43 Control: 38	Group 1: 47 Group 2: 47 Control: 46 *(median)*	Group 1: 20 (6-150) Group 2: 36 (6-154) Control: 16 (6-150) *(median and range)*	1: Hydrocortisone 25 mg and 1% lidocaine against tender point (2 ml fluid) (55% received 2 injections) 2: Triamcinolone 10 mg and 1% lidocaine (30% received 2 injections)	2 ml 1% lidocaine against tender point	Pain on VAS Tenderness score Pain-weigthed grip strength	24
Smidt et al. 2002 *General practice* *n=185*	Group 1: 55 (Group 2: 44) Control: 53	Group 1: 47 (Group 2: 48) Control: 46 *(median)*	Group 1: 11 (8-16) (Group 2: 11 (8-21)) Control: 11 (8-21) *(median and IQR)*	1: 10 mg triamcinolone and 1 ml lidocain againt all tender points up to 3 injections *2: One group reveived physiotherapy with ultrasound (not considered in this review)*	Wait-and-see (some were prescribed naproxen po 1000 mg daily)	Improvement on 6-point Likert scale Severity of complaint on scale Questionnaires PFGS Maximum grip strength (MGS) Pressue-pain measurements Satisfaction with treatment	52
Toker et al. 2008 *Outpatient clinic* *n=21*	43	45 (range 19-72)	not stated	One injection of 1 ml metylprednisolon and 1 ml prilocain with oral diklofenac 3 tablets (dose not stated) and etofenamat topically	Oral diklofenac 3 tablets (dose not stated) and etofenamat topically	Perceived abscense of pain Abscence of pain on palpation over lateral epicondyle and on isometric dorsiflection of wrist Pain score	4
Lindenhovius et al. 2008 *Outpatient clinic* *n=64*	Treatment: 63 Control: 60	Treatment: 50 +/- 8 Control: 51+/- 10	Treatment: 12 +/- 4 (2-20) Control: 8 +/- 4 (1-20)	4 mg dexamethasone and 10 mg lidocaine (2 ml fluid) against the most tender spot, fanning of the needle. One injection - but 6 of 64 got 2 injections.	10 mg lidocain, 2 ml fluid total	DASH questionnaire * Pain on VAS Grip strength	26
Newcomer et al. 2001 *Outpatient clinic* *n=39*	51	Treatment: 46.0 +/- 7.0 Control: 44.6+/- 7.6	Treatment: 3.2 (mean) SD 0.8 Control: 3.4 (mean) SD 0.9	One injection of 5 ml 4:1 0.25% bupivacaine and 6 mg/ml betamethasone against tender point. Home excercises consisting of ice massage, wrist stretching and progressive eccentric and concentric exercises	Placeboinjection of 5 ml bupivacaine Home excercises consisting of ice massage, wrist stretching and progressive eccentric and concentric exercises	Pain on VAS Functional pain questionnaire (PFGS at 4 and 8 weeks)	26
M-Silvestrini et al. 2005 *Outpatient clinic* *n=94*	47	45,5 +/- 7.7	more than 12	1: Concentric strengthening 3x10 repetitions once daily and wrist stretching twice daily for 6 weeks 2: Eccentric strengthening 3x10 repetitions once daily and wrist stretching twice daily for 6 weeks	Wrist stretching twice daily for 6 weeks	PFGS Pain on VAS PRFEQ questionnaire† Patient's log of training DASH questionnaire *	6
Peterson et al. 2011 *General practice* *n=81*	42	48	Treatment: 107 Control: 96	Three-month daily exercise regime performed at home with progressively increasing load on the extensor muscles	Information, wait-and-see	Pain on VAS during contraction and during elongation of forearm muscles Muscle strength with hand-held dynanometer DASH questionnaire	12
Selvanetti et al. 2003 *Setting not stated* *n=62*	Treatment: 45 Control: 48	Treatment: 41,3 Control: 40,5	Treatment: 28 (8-40) Control: 29 (12-44)	4 weeks home-exercise after instruction from physiotherapist consisting of stretching and eccentric excercise Counseling and use of elbow support	Sham ultrasound 20 sessions Counseling and use of elbow support	Ko scoring system (includes clench test, Thomsen test and pain). Verhaar scoring system on global improvement Subjective improvement VAS scale (0-100)	44 (24-56)

* DASH questionnaire (Disability of the Arm, Shoulder and Hand): an upper extremity specific health status measure.
† PRFEQ questionnaire: Patient-rated Forearm Evaluation Questionnaire
†† PRTEE questionnaire: Patient-Rated Tennis Elbow Score

Table 2: Quality rating of studies by assessing internal and external validity with the PEDro scale

		Study												
	PEDro criterion	**Bisset**	**Coombes**	**Hay**	**Price**	**Smidt**	**Toker**	**Lindenhovius**	**Newcomer**	**M-Silvestrini**	**Peterson**	**Selvanetti**	**Kochar**	**Tonks**
1	*eligibility criteria were specified*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*
2	subjects were randomly allocated to groups	1	1	1	1	1	1	1	1	1	1	1	1	1
3	allocation was concealed	1	1	1	0	1	0	1	0	0	1	1	0	1
4	the groups were similar at baseline regarding the most important prognostic indicators	1	1	1	1	1	1	1	1	1	1	1	1	0
5	there was blinding of all subjects	0	0	0	1	0	0	1	1	0	0	0	0	0
6	there was blinding of all therapists who administered the therapy	0	0	0	0	0	0	1	1	0	0	0	0	0
7	there was blinding of all assessors who measured at least one key outcome	1	1	1	1	1	0	1	0	0	0	0	0	0
8	measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	1	1	1	1	1	1	0	1	1	1	1	0	0
9	all subjects for whom outcome measures were available, received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	1	1	1	1	1	1	1	1	1	1	1	0	0
10	the results of between-group statistical comparisons are reported for at least one key outcome	1	1	1	1	1	1	1	1	1	1	1	1	1
11	the study provides both point measures and measures of variability for at least one key outcome	1	1	1	1	1	1	1	1	1	1	1	1	1
	Total PEDro score *(Sum criteria 2 to 11, maximum score is 10)*	**8**	**8**	**8**	**8**	**8**	**6**	**9**	**8**	**6**	**7**	**7**	**4** ***EXLUDED***	**4** ***EXLUDED***

Table 3. Effect size of improvement rate, reduction in pain and increase in grip strength for corticosteroid injection

	Short term 4-12 weeks	Intermediate term 26 weeks	Long term 52 weeks
Overall improvement RR (95% CI) RR>1 favours treatment			
Corticosteroid injection (CSI) vs no intervention or NSAIDs			
Bisset	2.94 (1.90 to 4.45)*	0.55 (0.41 to 0.73)*	0.75 (0.62 to 0.90)*
Coombes	7.32 (2.83 to 18.94)*	0.68 (0.50 to 0.92)*	0.91 (0.77 to 1.06)
Hay	1.60 (1.18 to 2.17)*	0.77 (0.60 to 0.98)*	1.07 (0.88 to 1.30)
Smidt	2.86 (1.96 to 4.16)*	-	0.84 (0.68 to 1.02)
Toker	2.27 (1.04 to 4.97)*	-	-
Pooled	-	0.66 (0.53 to 0.81)*	0.87 (0.73 to 1.04)
Heterogeneity	*>65%*	*p=0.21 I^2=35%*	*p=0.07 I^2=58%*
CSI vs lidocaine injection			
Lindenhovius	-	-	-
Price	-	-	-
CSI, excercise and stretching vs excersise and stretching			
Newcomer	-	-	-
Pain (negative value favours treatment) SMD (95% CI)			
CSI vs no intervention or NSAIDs			
Bisset	-1.43 (-1.83 to -1.04)*	0.40 (0.04 to 0.76)*	0.27 (-0.08 to 0.62)
Coombes	-2.14 (-2.68 to -1.60)*	0.16 (-0.28 to 0.59)	0.08 (-0.35 to 0.52)
Hay	-1.05 (-1.45 to -0.66)*	0.42 (0.04 to 0.80)*	1.35 (0.94 to 1.76)*
Smidt	-1.49 -(1.89 to -1.08)*	0.27 (-0.09 to 0.63)	0.15 (-0.20 to 0.51)
Toker	-1.14 (-2.07 to -0.22)*	-	-
Pooled	-1.43 (-1.64 to -1.23)*	0.32 (0.13 to 0.51)*	-
Heterogeneity	*p=0.032 I^2=62%*	*p=0.79 I^2=0%*	*>65%*
CSI vs lidocaine injection			
Lindenhovius	-0.25 (-0.74 to 0.24)	0.27 (-0.30 to 0.84)	-
Price 1	-1.06 (-1.63 to -0.49)*	3.13 (2.31 to 3.95)*	-
Price 2	-3.37 (-4.20 to -2.54)*	1.55 (0.93 to 2.17)*	-
Pooled	-	-	-
Heterogeneity	*>65%*	*>65%*	-
All above pooled	-	-	
Heterogeneity	*>65%*	*>65%*	
CSI, excercise and stretching vs excersise and stretching			
Newcomer[+]	0.16 (-0.49 to 0.81)	-0.37 (-1.04 to 0.30)	-
Maximum grip strength (positive value favours treatment) SMD (95% CI)			
CSI vs no intervention or NSAIDs			
Bisset	-	-	-
Coombes	-	-	-
Hay	-	-	-
Smidt	-1.42 (-1.82 to -1.03)*	-0.38 (-0.74 to -0.02)*	-0.36 (-0.72 to 0.002)
Toker	-	-	-
no pooling	-	-	-
CSI vs lidocaine injection			
Lindenhovius	-0.19 (-0.68 to 0.30)	0.07 (-0.50 to 0.64)	-
Price 1	-0.06 (-0.59 to 0.48)	-0.98 (-1,58 to -0.38)*	-
Price 2	2.31 (1.62 to 3.00)*	-0.86 (-1.44 to -0.29)*	-
Pooled	-	-	
Heterogeneity	*>65%*	*>65%*	
All above pooled	-	-0.48 (-0.73 to -0.24)*	-
Heterogeneity	*>65%*	*p=0.04 I^2=64%*	-
CSI, excercise and stretching vs excersise and stretching			
Newcomer[+]	-0.17 (-0.61 to 0.27)	-	-

**: statistically significant (p<0.05)* [+]*: The values for Newcomer are given as change in pain and and change in pain free grip strength*

Price 1: hydrocortisone vs. lidocaine

Price 2: triamcinolone vs lidocaine

Table 4. Effect sizes of treatment effects for non-electrotherapeutic physiotherapy

	Short term 4-12 weeks	Intermediate term 26 weeks	Long term 52 weeks
Manipulation and exercise vs no intervention			
Overall improvement RR (relative risk) (95% CI) - RR>1 favours treatment			
Bisset	2.44 (1.54 to 3.85)*	0.94 (0.78 to 1.12)	1.04 (0.93 to 1.15)
Coombes	4.00 (1.46 to 10.94)*	1.06 (0.89 to 1.28)	1.08 (0.99 to 1.18)
Pooled	2.75 (2.09 to 3.62)*	0.99 (0.75 to 1.30)	1.05 (0.75 to 1.49)
Heterogeneity	*p=0.37 I^2=0%*	*p=0.33 I^2=0%*	*p=0.57 I^2=0%*
Pain SMD (standardised mean difference) (95% CI) - negative value favours treatment			
Bisset	-0.63 (-0.99 to -0.27)*	-0.25 (-0.62 to 0.11)	-0.38 (-0.74 to -0.03)*
Coombes	-1.27 (-1.74 to -0.79)*	0.00 (-0.44 to 0.44)	0.00 (-0.44 to 0.44)
Pooled	-	-0.15 (-0.43 to 0.13)	-0.23 (-0.51 to 0.04)
Heterogeneity	*p>65%*	*p=0.39 I^2=0%*	*p=0.18 I^2=45%*
Pain free grip strength ratio affected/ unaffected arm SMD (95%)			
Bisset	0.76 (0.39 to 1.13)*	0.20 (-0.47 to 0.56)	0.17 (-0.18 to 0.52)
Coombes	-	-	-
Exercise vs no intervention			
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95%)			
Peterson	-0.03 (-0.47 to 0.40)	-	-
Pain on maximum voluntary contraction SMD (95% CI) - negative value favours treatment			
Peterson	-0.30 (-0.74 to 0.14)	-	-
Pain on maximum muscular elongation SMD (95% CI) - negative value favours treatment			
Peterson	-0.24 (-0.68 to 0.19)	-	-
Eccentric excercise and stretching vs stretching			
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95%)			
M-Silvestrini	-0.07 (-0.46 to 0.60)	-	-
Pain SMD (95% CI) - negative value favours treatment			
M-Silvestrini	-0.04 (-0.57 to 0.49)	-	-
Pain free grip strength affected arm SMD (95%)			
M-Silvestrini	-0.26 (-0.79 to 0.27)	-	-
Concentric excercise and stretching vs stretching			
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95%)			
M-Silvestrini	0.14 (-0.39 to 0.68)	-	-
Pain SMD (95% CI) - negative value favours treatment			
M-Silvestrini	0.41 (-0.13 to 0.95)	-	-
Pain free grip strength affected arm SMD (95%)			
M-Silvestrini	-0.34 (-0.88 to 0.20)	-	-
Eccentric excercise and stretching vs no intervention (sham ultrasound, elbow support)			
Overall improvement RR (95% CI) - RR>1 favours treatment			
Selvanetti	-	-	23.39 (3.38 to 161.70)*
Pain on Ko-scale (larger value means less pain) SMD (95% CI)			
Selvanetti	4.45 (3.51 to 5.40)*	-	4.65 (3.68 to 5.63)*
Grip strength on Ko-scale (larger value means greater strength) SMD (95%)			
Selvanetti	3.16 (2.40 to 3.92)*	-	3.65 (2.82 to 4.47)*

*: statistically significant (p<0.05)

BMJ open

Treating lateral epicondylitis with corticosteroid injections or non-electrotherapeutical physiotherapy: a systematic review

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-003564.R1
Article Type:	Research
Date Submitted by the Author:	27-Aug-2013
Complete List of Authors:	Olaussen, Morten; University of Oslo, Department of General Practice Holmedal, Oeystein; University of Oslo, Department of General Practice Lindbaek, Morten; University of Oslo, Department of General Practice Brage, Soeren; University of Oslo, Department of Community Health Solvang, Hiroko; University of Oslo, Department of General Practice
Primary Subject Heading:	Sports and exercise medicine
Secondary Subject Heading:	General practice / Family practice
Keywords:	SPORTS MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, Elbow & shoulder < ORTHOPAEDIC & TRAUMA SURGERY

Abstract

Objectives

To evaluate the current evidence for the efficacy of corticosteroid injection and non-electrotherapeutic physiotherapy compared with control for treating lateral epicondylitis.

Design

Systematic review.

Setting

n/a

Participants

We searched five databases in September 2012 for randomized, controlled studies with a minimum quality rating. Of 640 studies retrieved, eleven were included, representing 1161 patients of both sexes and all ages.

Interventions

Corticosteroid injection and non-electrotherapeutic physiotherapy.

Outcome measures

Relative risk (RR) or standardised mean difference (SMD) for overall improvement, pain and grip strength at 4 to 12, 26 and 52 weeks follow-up.

Results

Corticosteroid injection gave a short-term reduction in pain vs no intervention or NSAIDs (SMD -1.43, 95% CI -1.64 to -1.23). At intermediate follow-up, we found an increase in pain (SMD 0.32, 95% CI 0.13 to 0.51), reduction in grip-strength (SMD -0.48, 95% CI -0.73 to -

0.24), and negative effect on overall improvement effect (RR 0.66 (0.53 to 0.81). For corticosteroid injection vs lidocaine injection, evidence was conflicting. At long-term follow up, there was no difference on overall improvement and grip strength, with conflicting evidence for pain. Manipulation and exercise vs no intervention showed beneficial effect at short-term follow-up (overall improvement RR 2.75, 95% CI 1.30 to 5.82), but no significant difference at intermediate or long-term. We found moderate evidence for a short- and long-term effect of eccentric exercise and stretching vs no intervention. For exercise vs no intervention and eccentric or concentric exercise and stretching vs stretching alone, we found moderate evidence of no short-term effect.

Conclusions

Corticosteroid injections have a short-term beneficial effect on lateral epicondylitis, but a negative effect at intermediate term. Evidence on long-term effect is conflicting. Manipulation and exercise and exercise and stretching have a short-term effect, the latter also a long-term effect.

Trial registration

None.

Article summary

Article focus

- What is the current evidence for the effect of treating lateral epicondylitis with corticosteroid injection or non-electrotherapeutic physiotherapy compared to control?

Key Messages

- Corticosteroid injections have a short-term beneficial effect on lateral epicondylitis, but a negative effect at intermediate term. Evidence on long-term effect is conflicting.
- There is evidence for a short-term effect of manipulation and exercise and exercise and stretching, for the latter also on long-term.

Strengths and limitations of this review

- We found overall few good quality studies on these treatments, making a meta-analysis possible only for a few studies and outcomes.

Introduction

Lateral epicondylitis of the elbow is a frequently encountered complaint in general practice with an incidence of 4 - 7 per 1000 per year [1-3]. It is characterised by pain and tenderness over the lateral humeral epicondyle and pain on resisted dorsiflexion and radial deviation of the wrist. It is usually a self-limiting condition, often resolving in 6 to 12 months regardless of treatment, but complaints may last up to 2 years or longer [4]. Due to considerable pain and discomfort, many patients need time off from work.

Most authors attribute the condition to a lesion in the short radial extensor muscle [1, 5]. A recent study has found evidence of reduced hyperaemia measured with spectral and colour Doppler in lateral epicondylitis treated with corticosteroid injection, suggesting evidence of an inflammatory component [6]. Others, finding little evidence of inflammation have proposed the term "lateral epicondylalgia" for the condition [7].

Most patients with lateral epicondylitis are treated in general practice, and although a large number of treatments are in use, there is no consensus on which treatments are most effective. The Cochrane Library has reviewed several treatments. For topical NSAIDs and NSAIDs taken orally, the conclusion is that both may have a short term effect [8]. For extracorporeal shockwave therapy, a review of nine studies including 1000 patients found this treatment to have no effect [9]. For acupuncture [10], deep friction massage [11], orthosis [12] and surgery [13] the reviews were inconclusive due to few and methodologically weak studies.

Four review articles have been published on the effect of corticosteroid injections [14-17]. They found a short-term effect of corticosteroid injection, but no proven long-term effect, and one review found evidence of a negative long-term effect [15]. However, some of the reviews included non-controlled studies [14, 16] and non-randomised studies [16]. In one

review [15], four of 12 included studies had no control group and one was a small pilot study with short follow up. Based on this, we find the evidence in published reviews on the long-term effect of corticosteroid injections to be conflicting.

Five reviews of physiotherapeutic interventions show that there are few published studies on the effect of non-electrotherapeutic treatment, and many have methodological weaknesses [16, 18-21]. Bisset et al. [18] found evidence that manipulation and exercise had a short term effect. Four other reviews [16, 19-21] found short-term effects of mobilisation, manipulation and exercise. Three of these reviews included non-randomised or non-controlled studies [16, 19, 21]. Most previous systematic reviews have included electrotherapeutic physiotherapy such as ultrasound and extra-corporeal shockwave [14, 16, 20, 21].

Since there is no established, well-documented treatment to which new treatments can be compared, the use of a control group is important. The natural course of the condition, where most patients eventually recover regardless of intervention, makes this even more necessary. In a comparison of two different treatments, any effect found may only reflect this natural course of recovery unless the treatments prove better than a control group with no treatment.

It has been shown that systematic reviews which include studies with low scores on internal validity may over-estimate effect sizes, thus introducing a potential bias to the review [22]. There may also be a problem using rating scales with heterogeneous criteria, including i.e. criteria related to external validity, interpretation or ethical issues [22, 23].

To address these issues, a new systematic review on non-electrotherapeutic physiotherapy and corticosteroid injection seemed warranted. We wanted to include only randomised studies with a control group with no treatment or studies in which the groups only differed in regards to the investigated treatment. An established quality rating scale would be

used. We also wanted to review the most current evidence on the efficacy of corticosteroid injection, since previous reviews have differing conclusions on long-term effect.

Objective

The aim of this review was to assess the current evidence for the efficacy of corticosteroid injection and non-electrotherapeutical physiotherapy compared with control in patients with tennis elbow.

Methods

We followed the recommendations of the Cochrane Collaboration [24] and the PRISMA Group [25] in the search and report of this systematic review.

Study selection

We used the following inclusion criteria:

Study type

Randomized, controlled trials assessing treatments for lateral epicondylitis or tennis elbow were eligible for inclusion. The studies had to have at least one treatment group and one control group. We defined a control group as a group receiving no treatment (a wait-and-see approach), common treatments with expected or known moderate effect (advice, rest, NSAIDs, pain-killers) or the same treatment as the experimental group with the exception of the investigated treatment.

Participants

All age groups with a clinical diagnosis of lateral epicondylitis were included without restriction on gender.

Treatments

We searched for studies investigating or comparing the efficacy of one of the following treatments: corticosteroid injection, non-electrotherapeutic physiotherapy including stretching, mobilisation, manipulation, massage, exercise or home training. Studies on splinting, ultrasound, shock wave and other electrotherapeutic modalities were excluded.

Outcome measures and follow up

At least one validated, patient-centred outcome was necessary. This could include outcomes important to the patient such as pain, range of movement, grip strength, work status and relevant functional questionnaires. We included only studies done in a clinical setting with at least four-week follow-up of treatment effect.

Study quality assessment

We used the 11-item PEDro scale to assess the quality of the studies included in the review. This rating system closely resembles the Cochrane Collaboration Scoring system [24] and is based on the Delphi list, developed for quality assessment of randomised controlled trials by Verhagen et al. [26]. It has been used in several previously published reviews [15, 18, 19]. The PEDro scale assesses the internal and external validity of a study by addressing the issues of eligibility criteria, randomisation, allocation, blinding, statistics and data reporting. The reliability of this scale has been confirmed by Maher et al in 2003 [27]. The maximum score is 10, since item number one on the scale (specified eligibility criteria) is not counted.

A minimum score of 5 out of 10 points (50%) was chosen to be necessary for inclusion in the review, as inclusion of lower quality studies in a systematic review may over-estimate the treatment effect of interventions [28]. Ten studies were independently assessed

by two researchers (MO, ØH) [29-38] and three studies were rated by both researchers together [39-41]. The final decision on PEDro score was reached by consensus.

Search methods for identification of studies

Electronic searches

From October 2009 to January 2010, we searched the following databases for publications: Medline (Ovid and PubMed), EVSCO/Cinahl, Embase, Allied and Complimentary Medicine, The Physiotherapy Evidence Database (PEDro) and the Cochrane RCT register. The searches within each database were done without restrictions on dates or languages. We used free text, not MESH terms, in these searches, and the key terms used were ”tennis elbow”, ”lateral epicondylitis”, epicondylalgia, elbow, randomised, randomized, injection, corticosteroid, and physiotherapy. The Boolean operator AND was used to link diagnostic terms and treatment where applicable. An additional search was done in September 2012 to identify any recently published studies.

Searching other resources

Further search was done in the reference list of articles initially considered for review.

Selection of studies

The searches resulted in a number of studies potentially eligible for inclusion. Titles and abstracts were then read by two researchers independently (MO, ØH) and potential studies were selected based on the inclusion criteria. The final decision on inclusion was made by consensus from reading the full-text documents.

Data extraction and statistical analysis

The included studies were read in full text and assessed by two independent researchers (MO, ØH). One article, published in Italian, was translated by a professional bureau [41]. A

standardized set of data was extracted from each selected study and recorded using standardized forms. We calculated statistics using the statistical computing language R (www.r-project.org, The R Foundation for Statistical Computing, Vienna, Austria). We reported the results of the outcome measures for three different timings of follow-up, defined as short-term (four to 12 weeks after randomisation), intermediate term (six months after randomisation) and long-term (more than six months after randomisation). For dichotomous data, we calculated relative risk (RR) and 95% confidence intervals (CI) with the R-project library "epi.R", for continuous data the standardised mean difference (SMD) and 95% CI with the R-project library "compute.es". We pooled estimates when we found sufficient clinical and statistical homogeneity between trials using the I^2 statistic, defined as I^2 less than 65% [42].

Some studies did not report the mean, standard deviation or number of samples, which were necessary to calculate SMD. Additional calculations were then required. For Coombes [38], the median and the interquartile range (IQR) were given. We set the median as the mean value and the standard deviation was given by IQR/1.35 under the assumption of normal distribution. For Newcomer [33], the standard deviation was calculated by t-statistics obtained by the p-value and degrees of freedom. For Price [34], the t-statistics was obtained by the degrees of freedom and 95% probability. The standard deviation was estimated by the t-statistics, the mean value and upper/lower confidence intervals.

For overall improvement, a RR larger than 1 favoured treatment, and was statistically significant if the CI excluded 1. We defined the effect as large for values larger than 2 or less than 0.5, medium between 0.5 and 0.8 and between 1.25 and 2 and small for values between 0.8 and 1.0 and between 1.0 and 1.25.

For continuous data, a positive or negative SMD favoured treatment depending on the outcome measures, ie. for pain a negative SMD favoured treatment and for grip strength a

positive SMD favoured treatment. SMD was statistically significant if the CI excluded zero. We defined the effect as large for SMD more than 0.8, medium between 0.5 and 0.8 and small for values less than 0.5. For outcomes that could not be pooled, we graded the strength of the scientific evidence as strong (consistent findings in several high-quality randomised controlled studies), moderate (one high-quality randomised controlled study), conflicting (inconsistent finding between many studies) or no evidence [43].

Inter-rater reliability

The inter-rater reliability for the individual PEDro scores was assessed by calculating the intra-class correlation coefficient [44]. The R-project library "psych" was used for this calculation. A substantial inter-rater reliability was found (intra-class correlation coefficient 0.69 (0.15-0.91), $p<0.01$).

Results

The search retrieved an initial 839 hits, representing 640 individual articles. The further selection process is outlined in Figure 1. 623 articles were excluded based on title and abstract in a preliminary review. 17 articles [29-37, 39, 41, 45-50] were then assessed using the full-text documents. Three were found not to be randomised controlled trials [45-47], two had a PEDro quality rating below 50% (Table 2) [37, 39] and three had a follow-up shorter than four weeks [48-50]. The additional search done in september 2012 retrieved two possible studies [40, 51], one of which was excluded for not having a control group [51]. A recently published study was also assessed [38] and a total of 11 studies were included in the final review [29-36, 38, 40, 41].

Included studies

The characteristics and details of each study are given in Table 1. The included studies represented a total population of 1161 patients. Several studies had more than one treatment

group, so the 11 included studies investigated 15 treatment groups relevant for this review. For the statistical analysis, one study which used two different corticosteroids, was treated as two studies [34].

The mean age of patients varied from 41 to 51 years and the female percentages varied from 35 to 63. There were large differences in duration of complaints at baseline between studies. Most had a duration of several weeks to months and only one stated a short duration [33]. Eight studies had control groups with no active treatment [29-31, 34-36, 38, 40], e.g. a wait-and-see group or NSAIDs. Two of these used lidocaine as a placebo injection [31, 34]. In the three other studies, the control and treatment groups both received similar active treatments, with the intervention group in addition receiving the treatment to be investigated [32, 33, 41] .

Eight studies investigated corticosteroid injections, representing 925 patients [29-31, 33-36, 38]. Five different corticosteroids were used, with different dosages and injection techniques. The control groups received no active treatment in seven of the eight studies, in one study both the control and treatment group received additional exercise treatment [33]. Seven of the studies had a long-time follow up of 24 weeks or more [29-31, 33-35, 38].

There were few studies covering non-electrotherapeutic physiotherapy. We found five studies which could be included, representing 600 patients [29, 32, 38, 40, 41]. The treatment modalities investigated were manipulation and exercise [29, 38], concentric or eccentric exercises [32], exercise [40] and eccentric exercises with stretching [41]. Three studies had a control group with no active treatment [29, 38, 40], the other two had control groups that received stretching and orthosis respectively. Three studies [29, 38, 41] had a follow up of 24 weeks or more.

The most frequently used outcome measures were assessment of pain and grip strength. Six studies measured pain free grip strength with handheld dynamometers [29-33,

35]. Eight studies used a number of different questionnaires covering pain, function and disability [29-33, 35, 38, 40]. Nine studies assessed pain on a visual analogue scale or Likert-scale [29-34, 36, 38, 40], and six studies rated patient's assessment of improvement on graded scales [29, 30, 35, 36, 38, 41].

Risk of bias in included studies

We addressed the issues of the quality of the included studies and completeness of reported data by rating them with the PEDro scale (Table 2). Most studies used a computerized randomisation schedule, and seven of the eleven studies used concealed allocation [29-31, 35, 38, 40, 41]. Baseline comparison was done in all studies, the dropout rate was below 15% in ten studies [29, 30, 32-36, 38, 40, 41] and intention to treat analysis was stated in all studies. There was between-group analysis of at least one outcome measure in all the studies, and both point-measures and variations of outcome measures were reported in all studies.

The use of blinding was more diverse among the studies. Blinding the subject for treatment is difficult for physiotherapeutic treatments, but the use of blinded assessors reduces the risk of bias. None of the studies on physiotherapy in our review had blinded subjects or therapists, but two used blinded assessors [29, 38]. This might give biased results in the studies covering physiotherapeutic treatments.

For the eight studies on corticosteroid injection, the number using blinding was larger. There was blinding of subjects in four studies [31, 33, 34, 38], of the treating doctor in two [31, 33] and of assessors in six studies [29-31, 34, 35, 38].

In several studies the control group received some form of treatment (although similar to the treatment group) [32-34, 36, 41]. In these studies, synergistic effects between the treatments cannot be ruled out. This makes the results more difficult to interpret. Two studies had a short follow up of four and six weeks [32, 36], which for a condition usually lasting

several months, reduces the clinical implication of the results. Difference in duration of complaints at baseline also complicates comparison between studies.

Effects of interventions

Corticosteroid injection

The efficacy of corticosteroid injection for treating lateral epicondylitis was investigated in eight studies (Table 3 and Figure 2 [52]). For short-term follow up, heterogeneity between studies made pooling of outcomes only possible for pain. For corticosteroid injection vs no intervention or NSAIDs, we found strong evidence for a beneficial effect on overall improvement and a large positive effect on pain [29, 30, 35, 36, 38]. For grip strength, we found moderate evidence for a negative effect [35]. For corticosteroid injection vs lidocaine injection, evidence was conflicting for effect on pain, with two studies showing a large positive effect (Price et al. using hydrocortisone and triamcinolone) [34] and one showing no significant difference [31]. For maximum grip strength, the evidence was also conflicting, with one study showing a large postitive effect of treatment (Price et al. using triamcinolone)[34], and two studies showing no statistical difference (Lindenhovius, Price et al. using hydrocortisone) [31, 34]. For corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found moderate evidence for no significant difference on pain and grip strength [33].

At intermediate follow-up, we found sufficient homogeneity to poole estimates for overall improvement [29, 30, 38] and pain [29, 30, 35, 38] for corticosteroid injection vs. no intervention or NSAIDs. For overall improvement this showed a medium negative effect and for pain a small negative effect. For maximum grip strength, pooling of corticosteroid injection vs no intervention, NSAIDS and lidocaine showed a small negative effect [31, 34, 35]. For corticosteroid injection vs lidocaine injection, pooling of estimates was not possible due to heterogeneity. For pain, two studies showed a large negative effect (Price et al. using

hydrocortisone and triamcinolone)[34], and one study showed no significant difference [31], thus the evidence was conflicting. For grip strength, the evidence was also conflicting, with the same two studies showing a large negative effect [34] and one showing no significant difference [31]. For corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found moderate evidence of no significant effect on pain [33].

At long-term follow-up, pooled estimates of overall improvement showed no difference in effect of corticosteroid injection vs no intervention or NSAIDs [29, 30, 35, 38]. For pain, heterogeneity prevented pooling and we found the evidence conflicting with one study showing a large negative effect [30], and three others showing no significant difference in effect [29, 35, 38]. For grip strength, we found moderate evidence of no significant difference [35]. For corticosteroid injection vs lidocaine injection and corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found no data on long-term effect.

Physiotherapy

We included five studies (n=600) investigating non-electrotherapeutical physiotherapy, representing five different treatment modalities (Table 4 and Figure 3 [52]).

Two studies investigated the efficacy of manipulation and exercise vs. no intervention [29, 38]. At short-term, pooled estimates showed a large positive effect on overall improvement. For pain, pooling was not possible due to heterogeneity. We found strong evidence for a beneficial effect, for pain free grip strength we found moderate evidence for a beneficial effect. At intermediate-term, pooled estimates showed no difference between treatment and control for neither pain nor overall improvement. There was moderate evidence for no difference in pain free grip strength. At long-term, pooled estimates again showed no difference between treatment and control for either pain or improvement and we found moderate evidence for no difference in pain free grip strength.

The efficacy of exercise vs no intervention was investigated in one study [40]. We found moderate evidence for no short-term difference in effect for outcomes on pain and DASH-score. There was no data on intermediate- or long-term effect.

For eccentric exercise and stretching vs stretching, investigated in one study [32], we found moderate evidence for no short-term treatment effect for outcomes on pain, pain-free grip strength and DASH-score. There was no data on intermediate- or long-term effect.

The same study also investigated the efficacy of concentric exercise and stretching vs stretching. We found moderate evidence for no short-term treatment effect for outcomes on pain, pain-free grip strength and DASH-score. There was no data on intermediate- or long-term effect.

Eccentric exercise and stretching vs no intervention was investigated in one study [41]. We found moderate evidence for a positive effect on pain and grip strength at short-term follow up. There was no data on efficacy at intermediate follow-up, but at long-term, we found moderate evidence of a positive effect on overall improvement, pain and grip strength.

Discussion

Summary of main results

This review found overall evidence for a short-term beneficial effect of corticosteroid injection. At intermediate follow-up, the evidence showed an overall negative effect. For corticosteroid injection vs lidocaine injection, we found the evidence to be conflicting. At long-term follow up, the evidence suggest no difference in effect on overall improvement and grip strength, but the evidence was conflicting for pain. For manipulation and exercise vs no intervention, we found an overall beneficial effect at short term, but no significant difference at intermediate or long-term follow-up. The evidence on exercise vs no intervention showed no differences at short-term follow up. For eccentric exercise and stretching vs stretching

alone, the evidence showed no short-term difference in effect. The same was found for concentric exercise and stretching vs stretching. The evidence on eccentric exercise and stretching vs no intervention showed a beneficial effect at short-term and long-term, while there was no data on intermediate follow-up.

For treating lateral epicondylitis, this review showed evidence for a short-term benefit of corticosteroid injection and manipulation with exercise. Eccentric exercise and stretching showed beneficial effect both at short- and long-term follow-up.

Overall completeness and quality of the evidence

There is a paucity of well-designed studies for determining the effect of non-electrotherapeutic physiotherapy. The conclusions on the effect of these treatments are therefore limited. A comparison and review of several individual studies was only possible for one treatment modality, manipulation and exercise vs no intervention (Table 4).

We included eight studies treating a total of 925 patients with corticosteroid injections in our review. The conclusions for this treatment are more solid due to the larger number of studies, seven of which had long-term follow up. Due to differences in type of corticosteroids used, treatment regimes and outcome measures in the included studies, pooling of outcome measures was difficult. We found statistical heterogeneity for most outcomes, and pooling was only possible for a few of the outcomes and follow-ups. The long-term effect of corticosteroid injection showed conflicting results in the included studies. The large differences across the studies in duration of complaints at baseline, corticosteroids used in different dosages, and control group treatments may explain this.

The difference in duration of complaints at baseline complicates the interpretation and comparison of the results, since there might be different effects of the treatments on an epicondylitis of recent onset compared to one that has lasted several months. This is also reflected by Cook [53] who considered tendinopathy as a continuum with three stages and

different characteristics and presumably treatments for each stage. Haahr [54] found that high physical strain at work, work with manual tasks, high perceived stress at baseline and a high level of pain and dysfunction seem to predict an unfavourable outcome after one year. Thus any differences in baseline characteristic for these parameters might possibly influence between-group differences of outcome.

Potential biases in the review process

The search process, selection of search terms and possible errors in reading and assessing the large number of articles represent a possible bias. Although we have searched several databases with a number of search terms, we may have missed some published studies. To reduce the risk of bias in the inclusion process, we used two reviewers who independently screened articles.

Our choice of inclusion criteria, especially the type of control or comparison treatment and the use of a cut-off quality score (PEDro), has important implications for the conclusions that can be drawn from this review. The efficacy of the treatments are here only compared with a control (no treatment) or to an underlying treatment that is common to both intervention groups, so no conclusion can be drawn on which of two different treatments is best.

To address the issue of publication bias, we searched two clinical trial registries: ClinicalTrial.gov (US National Institutes of Health) and Current Clinical Trials. We found no completed, unpublished studies on corticosteroid injection. Two completed studies on non-electrotherapeutic physiotherapy were found. One from The United Kingdom completed in 2008 on manipulation with movement and one from Sweden completed in 2009 on eccentric training. We have found no published articles from these studies. Unpublished studies are not indexed in PubMed or other databases and older studies may have been conducted without

registration in a clinical trial registry, making it difficult to make an overall assessment of publication bias.

Agreements and disagreements with other reviews

Our findings agree with earlier reviews [14, 16, 17, 55]. We found consistent evidence of a beneficial short-term effect of corticosteroid injections, but evidence on the long-term effect is still conflicting. Coombes et al. [15] found in their review that corticosteroid injections have a worse outcome in the long term than most conservative interventions for tendinopathies of different locations. The included studies in our review did not allow for a similar strong conclusion on the long-term effect of corticosteroid injections. For non-electrotherapeutical physiotherapy, we agree with earlier reviews [14, 16, 18, 19, 21] that there is moderate evidence of a short-term effect of manipulation and exercise. Our review strengthens this conclusion with the inclusion of a recently published study [40]. In addition, we found moderate evidence of both short- and long-term beneficial effect of eccentric exercise and stretching.

Authors' conclusions

Implications for practice

We found that both corticosteroid injection and manipulation with exercise gave a short-term benefit compared to control for treating lateral epicondylitis. At intermediate term, treatment with corticosteroid injection came out worse, while manipulation with exercise was not different from control. At long term, both treatments showed no benefit over control. For patients wanting treatment, it seems reasonable to recommend manipulation and exercise. For patients with mild symptoms, a wait-and-see approach would be appropriate. Though showing a large short-term benefit, the negative intermediate-term effect and uncertain long-term effect of corticosteroid injection make this treatment difficult to recommend. Eccentric

exercise with stretching showed efficacy both on short- and long-term follow-up, but only in one study.

Implications for research

We found few studies and some conflicting results on the long-term efficacy of corticosteroid injection. More trials or a meta-analysis with individual patient data from earlier studies might give better answers to the question on long-term effect.

For non-electrotherapeutical physiotherapy, more studies with a randomised, controlled design are needed. Blinding, for example by using a blinded assessor, should be applied wherever possible. The promising results of manipulation with exercise and eccentric exercise with stretching need further investigating.

Future studies should differentiate between acute and chronic complaints. Baseline levels of perceived pain, stress levels, handedness and presence of physical stress at work should be recorded. Standardization in the usage of outcome measures will enable data pooling and meta-analyses in future reviews. Studies investigating the combined effect of physiotherapy and corticosteroid injection treatments would also be useful. Most patients with acute lateral epicondylitis are treated in a general practice setting, and future research should be performed in such a setting.

Acknowledgements

Morten Olaussen and Oeystein Holmedal designed the study, performed the searches, read articles, decided which articles to include, performed the data extractions, interpreted the findings and wrote the main manuscript. Morten Lindbaek designed the study, decided which articles to include, interpreted the findings and revised the manuscript. Soeren Brage decided which articles to include, interpreted the findings and revised the manuscript. Hiroko Solvang

did the statistical calculations and analysis, interpreted the findings and revised the manuscript.

Competing interests

The authors declare that they have no competing interests.

Funding

Our work was funded by The Fund for General Practice Research, The Norwegian Medical Association, Oslo, Norway.

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FIGURES AND TABLES

uploaded as web only data:

Table 1: Demographics, treatments and outcome measures in the ten included studies

Table 2: Quality rating of included studies by assessing internal and external validity with the PEDro scale

Table 3: Effect size of improvement rate, reduction in pain and increase in grip strength for corticosteroid injection

Table 4: Effect size of treatment effects for non-electrotherapeutic physiotherapy

Figure 1: Outline of the selection process

Figure 2: Forest-plot of effect sizes for corticosteroid injection

Figure 3: Forest-plot of effect sizes for non-electrotherapeutic physiotherapy

Figure 1: Outline of the selection process

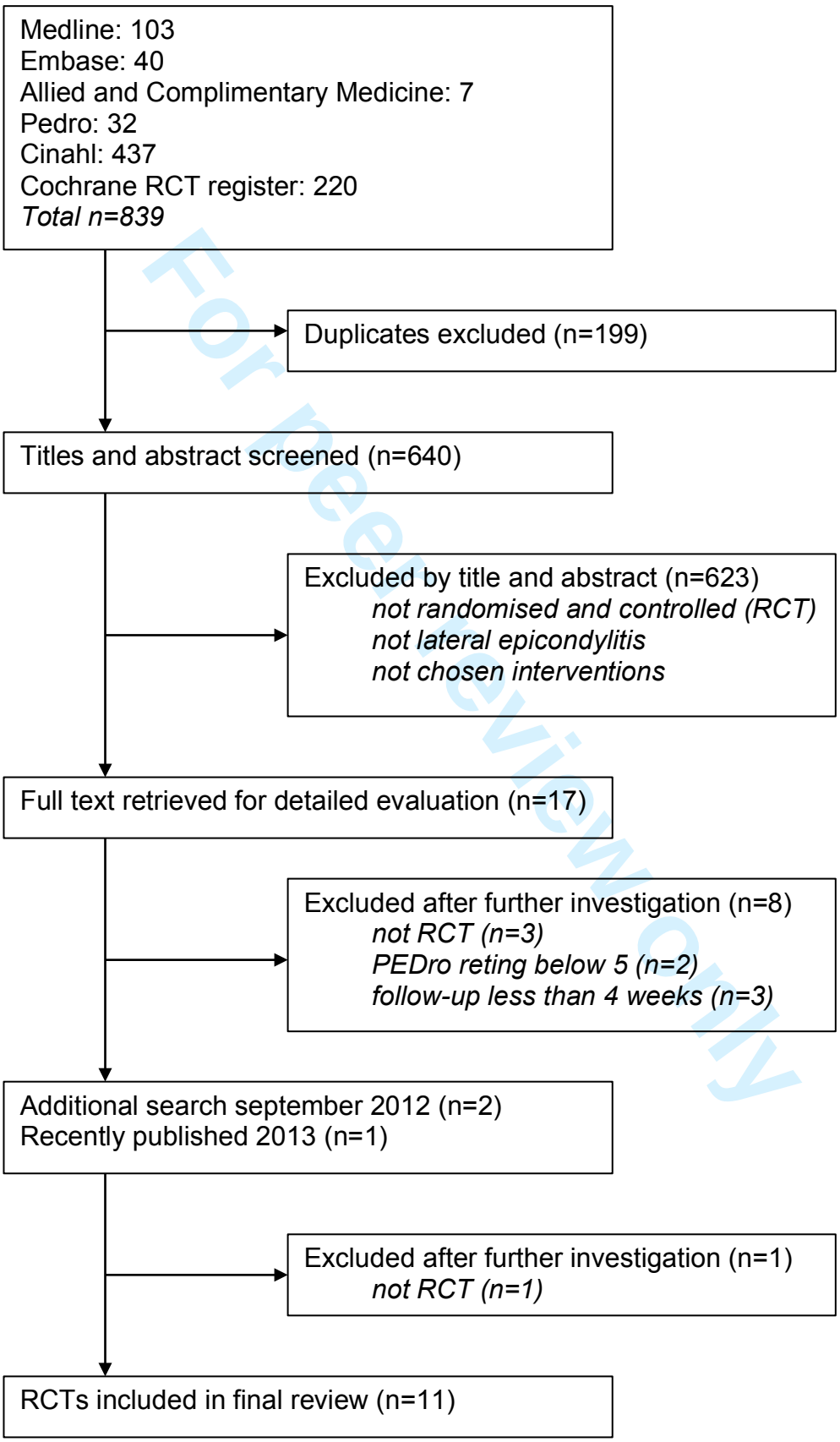
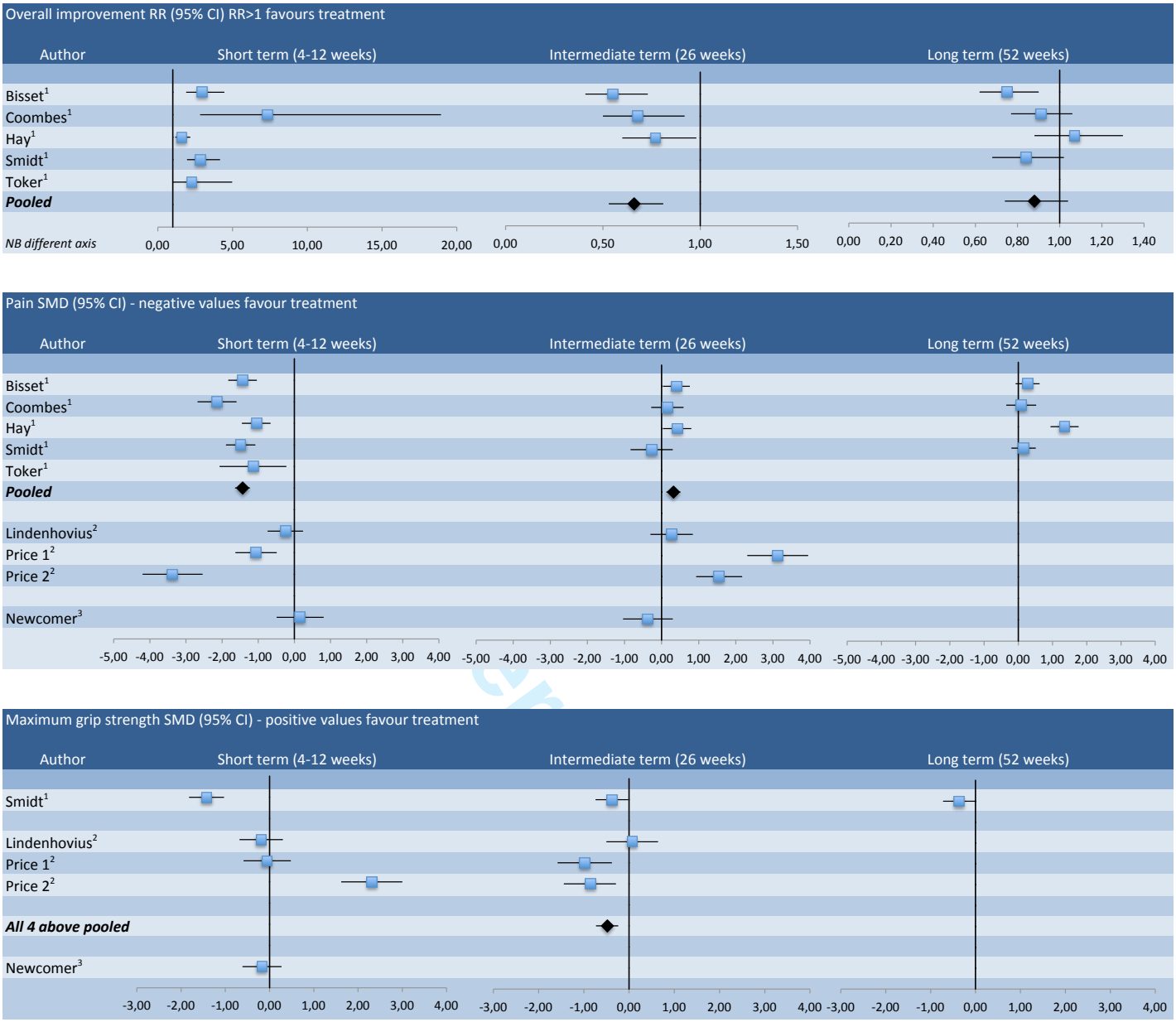


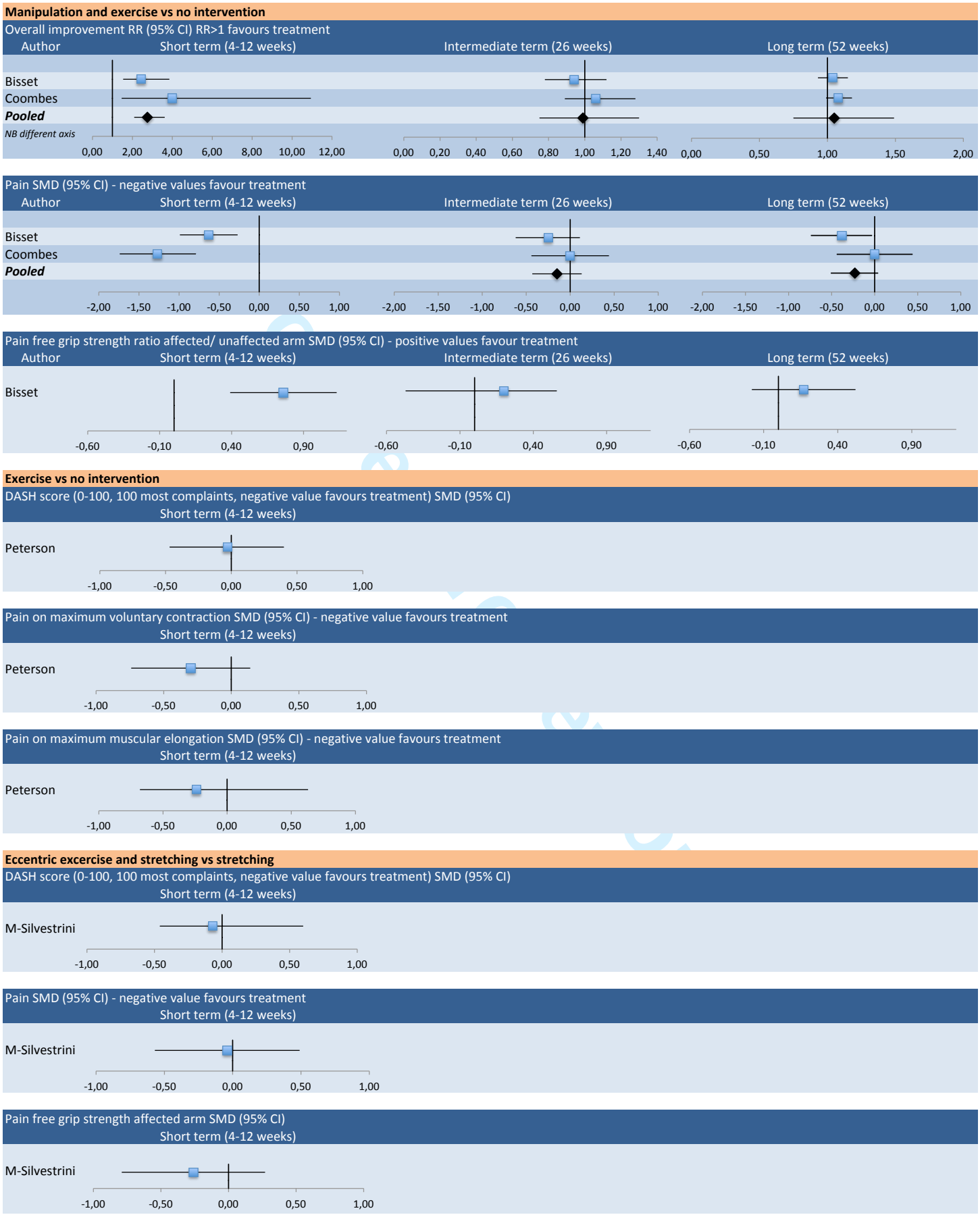
Figure 2. Forest-plot of effect sizes for corticosteroid injection



RR: relative risk
SMD: standardised mean difference
1: Corticosteroid injection (CSI) vs no intervention or NSAIDs
2: CSI vs lidocaine injection
3: CSI, excercise and stretching vs excersise and stretching. The values for Newcomer are given as change in pain and change in pain free grip strength.

Price 1: hydrocortisone vs lidocaine
Price 2: triamcinolone vs lidocaine

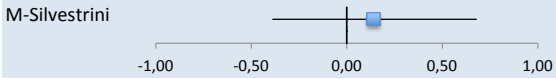
Figure 3. Forest-plot of effect sizes for non-electrotherapeutic physiotherapy



Concentric excercise and stretching vs stretching

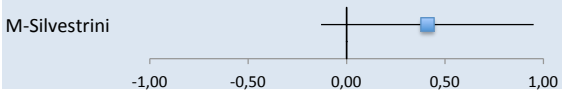
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95% CI)

Short term (4-12 weeks)



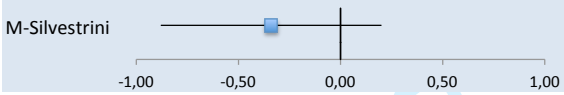
Pain SMD (95% CI) - negative value favours treatment

Short term (4-12 weeks)



Pain free grip strength affected arm SMD (95% CI)

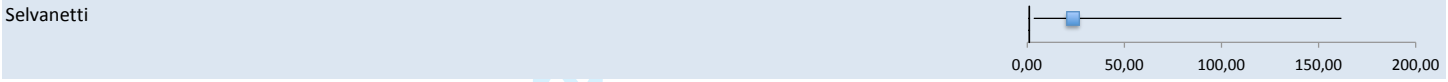
Short term (4-12 weeks)



Eccentric excercise and stretching vs no intervention (sham ultrasound, elbow support)

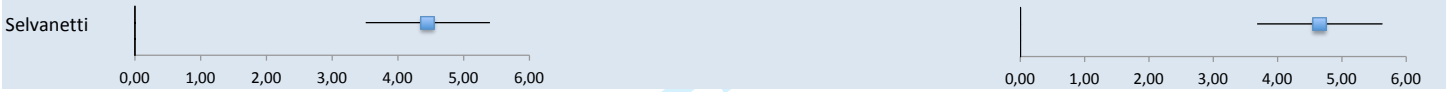
Improvement/success RR (95% CI) - RR>1 favours treatment

Short term (4-12 weeks) Intermediate term (26 weeks) Long term (52 weeks)



Pain on Ko-scale (larger value means less pain) SMD (95% CI)

Short term (4-12 weeks) Intermediate term (26 weeks) Long term (52 weeks)



Grip strength on Ko-scale (larger value means greater strength) SMD (95% CI)

Short term (4-12 weeks) Intermediate term (26 weeks) Long term (52 weeks)

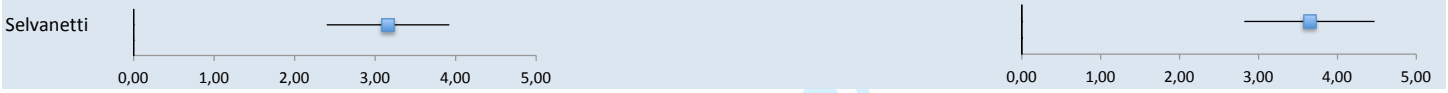


Table 1: Demographics, treatments and outcome measures in the eleven included studies

Study and year *setting and sample size*	Women *(percentages)*	Age *(mean if not otherwise stated)*	Duration of complaints *(weeks)*	Treatment groups	Control group	Outcome measures *(excerpts)*	Follow up *(weeks)*
Bisset et al. 2006 *Outpatient clinic* *n=198*	35	47,6 (SD 7.8)	22 (median) (IQR: 12-42)	1: 10 mg triamcinolone and 1 ml lidocaine against the most painful point repeated after 2weeks 2: Elbow manipulation (manipulation with mowement) and excercise 8 sessions of 30 minutes duration during a 6 week period and home exercise	Information, wait-and-see	Improvement on 6-point Likert-scale Pain free grip strength (PFGS) Assessed severity on VAS-scale (Visual Analogue Scale) Pain on VAS Pain free function questionnaire	52
Coombes et al. 2013 *Community setting* *n=165*	38	49.7 (SD 8.1)	16 (median) (IQR 10-26)	1: One injection of 1 ml triamcinolone 10 ml/ml and 1 ml lignocaine 1% against site of greatest palpable tenderness at the common extensor origin 2: Elbow manipulation (manipulation with mowement) and excercise 8 sessions of 30 minutes duration during a 8 week period and home exercise *3: One injection of triamcinolone followed by 8 sessions of elbow manipulation and excersie, home excercise for 8 weeks (not considered in this review)*	Placebo injection 0.5 ml 0.9 % isotonic saline	Improvement on 6-point Likert-scale One year recurrence Pain on VAS PRTEE questionnaire †† EuroQol-EQ-5D quality of life score	52
Hay et al. 1999 *General practice* *n=164*	Group 1: 41 (Group 2: 53) Control: 48	Age ≥ 45: (percentages) Group 1: 70 (Group 2: 68) Control: 38	9 (mean) Percentage with pain >3 months: Group 1: 36 (Group 2: 25) Control: 31	1: One injection of methylprednisolone 20 mg and 0.5 ml 1% lignocaine towards tender spot *2: Naproxen po 500 mg bid for 2 weeks (not considered in this review)*	Placebo tablets	Improvement on 5-point Likert-scale Pain on 10-point Likert-scale Function on 10-point Likert-scale Main complaint on 10-point Likert-scale Disability questionnaire PFGS	52
Price et al. 1991 *Outpatient clinic* *n=88*	Group 1: 48 Group 2: 43 Control: 38	Group 1: 47 Group 2: 47 Control: 46 *(median)*	Group 1: 20 (6-150) Group 2: 36 (6-154) Control: 16 (6-150) *(median and range)*	1: Hydrocortisone 25 mg and 1% lidocaine against tender point (2 ml fluid) (55% received 2 injections) 2: Triamcinolone 10 mg and 1% lidocaine (30% received 2 injections)	2 ml 1% lidocaine against tender point	Pain on VAS Tenderness score Pain-weigthed grip strength	24
Smidt et al. 2002 *General practice* *n=185*	Group 1: 55 (Group 2: 44) Control: 53	Group 1: 47 (Group 2: 48) Control: 46 *(median)*	Group 1: 11 (8-16) (Group 2: 11 (8-21)) Control: 11 (8-21) *(median and IQR)*	1: 10 mg triamcinolone and 1 ml lidocain againt all tender points up to 3 injections *2: One group reveived physiotherapy with ultrasound (not considered in this review)*	Wait-and-see (some were prescribed naproxen po 1000 mg daily)	Improvement on 6-point Likert scale Severity of complaint on scale Questionnaires PFGS Maximum grip strength (MGS) Pressue-pain measurements Satisfaction with treatment	52
Toker et al. 2008 *Outpatient clinic* *n=21*	43	45 (range 19-72)	not stated	One injection of 1 ml metylprednisolon and 1 ml prilocain with oral diklofenac 3 tablets (dose not stated) and etofenamat topically	Oral diklofenac 3 tablets (dose not stated) and etofenamat topically	Perceived abscense of pain Abscence of pain on palpation over lateral epicondyle and on isometric dorsiflection of wrist Pain score	4
Lindenhovius et al. 2008 *Outpatient clinic* *n=64*	Treatment: 63 Control: 60	Treatment: 50 +/- 8 Control: 51+/- 10	Treatment: 12 +/- 4 (2-20) Control: 8 +/- 4 (1-20)	4 mg dexamethasone and 10 mg lidocaine (2 ml fluid) against the most tender spot, fanning of the needle. One injection - but 6 of 64 got 2 injections.	10 mg lidocain, 2 ml fluid total	DASH questionnaire * Pain on VAS Grip strength	26
Newcomer et al. 2001 *Outpatient clinic* *n=39*	51	Treatment: 46.0 +/- 7.0 Control: 44.6+/- 7.6	Treatment: 3.2 (mean) SD 0.8 Control: 3.4 (mean) SD 0.9	One injection of 5 ml 4:1 0.25% bupivacaine and 6 mg/ml betamethasone against tender point. Home excercises consisting of ice massage, wrist stretching and progressive eccentric and concentric exercises	Placeboinjection of 5 ml bupivacaine Home excercises consisting of ice massage, wrist stretching and progressive eccentric and concentric exercises	Pain on VAS Functional pain questionnaire (PFGS at 4 and 8 weeks)	26
M-Silvestrini et al. 2005 *Outpatient clinic* *n=94*	47	45,5 +/- 7.7	more than 12	1: Concentric strengthening 3x10 repetitions once daily and wrist stretching twice daily for 6 weeks 2: Eccentric strengthening 3x10 repetitions once daily and wrist stretching twice daily for 6 weeks	Wrist stretching twice daily for 6 weeks	PFGS Pain on VAS PRFEQ questionnaire† Patient's log of training DASH questionnaire *	6
Peterson et al. 2011 *General practice* *n=81*	42	48	Treatment: 107 Control: 96	Three-month daily exercise regime performed at home with progressively increasing load on the extensor muscles	Information, wait-and-see	Pain on VAS during contraction and during elongation of forearm muscles Muscle strength with hand-held dynanometer DASH questionnaire	12
Selvanetti et al. 2003 *Setting not stated* *n=62*	Treatment: 45 Control: 48	Treatment: 41,3 Control: 40,5	Treatment: 28 (8-40) Control: 29 (12-44)	4 weeks home-exercise after instruction from physiotherapist consisting of stretching and eccentric excercise Counseling and use of elbow support	Sham ultrasound 20 sessions Counseling and use of elbow support	Ko scoring system (includes clench test, Thomsen test and pain). Verhaar scoring system on global improvement Subjective improvement VAS scale (0-100)	44 (24-56)

* DASH questionnaire (Disability of the Arm, Shoulder and Hand): an upper extremity specific health status measure.
† PRFEQ questionnaire: Patient-rated Forearm Evaluation Questionnaire
†† PRTEE questionnaire: Patient-Rated Tennis Elbow Score

Table 2: Quality rating of studies by assessing internal and external validity with the PEDro scale

		Study												
	PEDro criterion	**Bisset**	**Coombes**	**Hay**	**Price**	**Smidt**	**Toker**	**Lindenhovius**	**Newcomer**	**M-Silvestrini**	**Peterson**	**Selvanetti**	**Kochar**	**Tonks**
1	*eligibility criteria were specified*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*
2	subjects were randomly allocated to groups	1	1	1	1	1	1	1	1	1	1	1	1	1
3	allocation was concealed	1	1	1	0	1	0	1	0	0	1	1	0	1
4	the groups were similar at baseline regarding the most important prognostic indicators	1	1	1	1	1	1	1	1	1	1	1	1	0
5	there was blinding of all subjects	0	0	0	1	0	0	1	1	0	0	0	0	0
6	there was blinding of all therapists who administered the therapy	0	0	0	0	0	0	1	1	0	0	0	0	0
7	there was blinding of all assessors who measured at least one key outcome	1	1	1	1	1	0	1	0	0	0	0	0	0
8	measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups	1	1	1	1	1	1	0	1	1	1	1	0	0
9	all subjects for whom outcome measures were available, received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by "intention to treat"	1	1	1	1	1	1	1	1	1	1	1	0	0
10	the results of between-group statistical comparisons are reported for at least one key outcome	1	1	1	1	1	1	1	1	1	1	1	1	1
11	the study provides both point measures and measures of variability for at least one key outcome	1	1	1	1	1	1	1	1	1	1	1	1	1
	Total PEDro score *(Sum criteria 2 to 11, maximum score is 10)*	**8**	**8**	**8**	**8**	**8**	**6**	**9**	**8**	**6**	**7**	**7**	**4** ***EXLUDED***	**4** ***EXLUDED***

Table 3. Effect size of improvement rate, reduction in pain and increase in grip strength for corticosteroid injection

	Short term 4-12 weeks	Intermediate term 26 weeks	Long term 52 weeks
Overall improvement RR (95% CI) RR>1 favours treatment			
Corticosteroid injection (CSI) vs no intervention or NSAIDs			
Bisset	2.94 (1.90 to 4.45)*	0.55 (0.41 to 0.73)*	0.75 (0.62 to 0.90)*
Coombes	7.32 (2.83 to 18.94)*	0.68 (0.50 to 0.92)*	0.91 (0.77 to 1.06)
Hay	1.60 (1.18 to 2.17)*	0.77 (0.60 to 0.98)*	1.07 (0.88 to 1.30)
Smidt	2.86 (1.96 to 4.16)*	-	0.84 (0.68 to 1.02)
Toker	2.27 (1.04 to 4.97)*	-	-
Pooled	-	0.66 (0.53 to 0.81)*	0.87 (0.73 to 1.04)
Heterogeneity	*>65%*	*p=0.21 I^2=35%*	*p=0.07 I^2=58%*
Pain (negative value favours treatment) SMD (95% CI)			
CSI vs no intervention or NSAIDs			
Bisset	-1.43 (-1.83 to -1.04)*	0.40 (0.04 to 0.76)*	0.27 (-0.08 to 0.62)
Coombes	-2.14 (-2.68 to -1.60)*	0.16 (-0.28 to 0.59)	0.08 (-0.35 to 0.52)
Hay	-1.05 (-1.45 to -0.66)*	0.42 (0.04 to 0.80)*	1.35 (0.94 to 1.76)*
Smidt	-1.49 -(1.89 to -1.08)*	0.27 (-0.09 to 0.63)	0.15 (-0.20 to 0.51)
Toker	-1.14 (-2.07 to -0.22)*	-	-
Pooled	-1.43 (-1.64 to -1.23)*	0.32 (0.13 to 0.51)*	-
Heterogeneity	*p=0.032 I^2=62%*	*p=0.79 I^2=0%*	*>65%*
CSI vs lidocaine injection			
Lindenhovius	-0.25 (-0.74 to 0.24)	0.27 (-0.30 to 0.84)	-
Price 1	-1.06 (-1.63 to -0.49)*	3.13 (2.31 to 3.95)*	-
Price 2	-3.37 (-4.20 to -2.54)*	1.55 (0.93 to 2.17)*	-
Pooled	-	-	-
Heterogeneity	*>65%*	*>65%*	-
All above pooled	-	-	
Heterogeneity	*>65%*	*>65%*	
CSI, excercise and stretching vs excersise and stretching			
Newcomer[+]	0.16 (-0.49 to 0.81)	-0.37 (-1.04 to 0.30)	-
Maximum grip strength (positive value favours treatment) SMD (95% CI)			
CSI vs no intervention or NSAIDs			
Smidt	-1.42 (-1.82 to -1.03)*	-0.38 (-0.74 to -0.02)*	-0.36 (-0.72 to 0.002)
no pooling	-	-	-
CSI vs lidocaine injection			
Lindenhovius	-0.19 (-0.68 to 0.30)	0.07 (-0.50 to 0.64)	-
Price 1	-0.06 (-0.59 to 0.48)	-0.98 (-1,58 to -0.38)*	-
Price 2	2.31 (1.62 to 3.00)*	-0.86 (-1.44 to -0.29)*	-
Pooled	-	-	
Heterogeneity	*>65%*	*>65%*	
All above pooled	-	-0.48 (-0.73 to -0.24)*	-
Heterogeneity	*>65%*	*p=0.04 I^2=64%*	-
CSI, excercise and stretching vs excersise and stretching			
Newcomer[+]	-0.17 (-0.61 to 0.27)	-	-

**: statistically significant (p<0.05)*
Price 1: hydrocortisone vs. lidocaine
Price 2: triamcinolone vs lidocaine
[+]: The values for Newcomer are given as change in pain and and change in pain free grip strength

Table 4. Effect sizes of treatment effects for non-electrotherapeutic physiotherapy

	Short term 4-12 weeks	Intermediate term 26 weeks	Long term 52 weeks
Manipulation and exercise vs no intervention			
Overall improvement RR (relative risk) (95% CI) - RR>1 favours treatment			
Bisset	2.44 (1.54 to 3.85)*	0.94 (0.78 to 1.12)	1.04 (0.93 to 1.15)
Coombes	4.00 (1.46 to 10.94)*	1.06 (0.89 to 1.28)	1.08 (0.99 to 1.18)
Pooled	2.75 (2.09 to 3.62)*	0.99 (0.75 to 1.30)	1.05 (0.75 to 1.49)
Heterogeneity	*p=0.37 I^2=0%*	*p=0.33 I^2=0%*	*p=0.57 I^2=0%*
Pain SMD (standardised mean difference) (95% CI) - negative value favours treatment			
Bisset	-0.63 (-0.99 to -0.27)*	-0.25 (-0.62 to 0.11)	-0.38 (-0.74 to -0.03)*
Coombes	-1.27 (-1.74 to -0.79)*	0.00 (-0.44 to 0.44)	0.00 (-0.44 to 0.44)
Pooled	-	-0.15 (-0.43 to 0.13)	-0.23 (-0.51 to 0.04)
Heterogeneity	*p>65%*	*p=0.39 I^2=0%*	*p=0.18 I^2=45%*
Pain free grip strength ratio affected/ unaffected arm SMD (95%)			
Bisset	0.76 (0.39 to 1.13)*	0.20 (-0.47 to 0.56)	0.17 (-0.18 to 0.52)
Exercise vs no intervention			
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95% CI)			
Peterson	-0.03 (-0.47 to 0.40)	-	-
Pain on maximum voluntary contraction SMD (95% CI) - negative value favours treatment			
Peterson	-0.30 (-0.74 to 0.14)	-	-
Pain on maximum muscular elongation SMD (95% CI) - negative value favours treatment			
Peterson	-0.24 (-0.68 to 0.19)	-	-
Eccentric excercise and stretching vs stretching			
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95% CI)			
M-Silvestrini	-0.07 (-0.46 to 0.60)	-	-
Pain SMD (95% CI) - negative value favours treatment			
M-Silvestrini	-0.04 (-0.57 to 0.49)	-	-
Pain free grip strength affected arm SMD (95%)			
M-Silvestrini	-0.26 (-0.79 to 0.27)	-	-
Concentric excercise and stretching vs stretching			
DASH score (0-100, 100 most complaints, negative value favours treatment) SMD (95% CI)			
M-Silvestrini	0.14 (-0.39 to 0.68)	-	-
Pain SMD (95% CI) - negative value favours treatment			
M-Silvestrini	0.41 (-0.13 to 0.95)	-	-
Pain free grip strength affected arm SMD (95% Ci)			
M-Silvestrini	-0.34 (-0.88 to 0.20)	-	-
Eccentric excercise and stretching vs no intervention (sham ultrasound, elbow support)			
Overall improvement RR (95% CI) - RR>1 favours treatment			
Selvanetti	-	-	23.39 (3.38 to 161.70)*
Pain on Ko-scale (larger value means less pain) SMD (95% CI)			
Selvanetti	4.45 (3.51 to 5.40)*	-	4.65 (3.68 to 5.63)*
Grip strength on Ko-scale (larger value means greater strength) SMD (95% CI)			
Selvanetti	3.16 (2.40 to 3.92)*	-	3.65 (2.82 to 4.47)*

*: statistically significant (p<0.05)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	in title
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	in abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	8
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	8
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6-8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	8-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	8-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	12
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8-10

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	17
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	na
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	10, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	10-12, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12, Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	13-15, table 3,4, figure 2,3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	13-15. table 3,4, figure 2,3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10,12,17,
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	na
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16-18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18-19
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	20

PRISMA 2009 Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Abstract

Objectives

To evaluate the current evidence for the efficacy of corticosteroid injection and non-electrotherapeutic physiotherapy compared with control for treating lateral epicondylitis.

Design

Systematic review.

Setting

n/a

Participants

We searched five databases in September 2012 for randomized, controlled studies with a minimum quality rating. Of 640 studies retrieved, eleven were included, representing 1161 patients of both sexes and all ages.

Interventions

Corticosteroid injection and non-electrotherapeutic physiotherapy.

Outcome measures

Relative risk (RR) or standardised mean difference (SMD) for overall improvement, pain and grip strength at 4 to 12, 26 and 52 weeks follow-up.

Results

Corticosteroid injection gave a short-term reduction in pain vs no intervention or NSAIDs (SMD -1.43, 95% CI -1.64 to -1.23). At intermediate follow-up, we found an increase in pain (SMD 0.32, 95% CI 0.13 to 0.51), reduction in grip-strength (SMD -0.48, 95% CI -0.73 to -

0.24), and negative effect on overall improvement effect (RR 0.66 (0.53 to 0.81). For corticosteroid injection vs lidocaine injection, evidence was conflicting. At long-term follow up, there was no difference on overall improvement and grip strength, with conflicting evidence for pain. Manipulation and exercise vs no intervention showed beneficial effect at short-term follow-up (overall improvement RR 2.75, 95% CI 1.30 to 5.82), but no significant difference at intermediate or long-term. We found moderate evidence for a short- and long-term effect of eccentric exercise and stretching vs no intervention. For exercise vs no intervention and eccentric or concentric exercise and stretching vs stretching alone, we found moderate evidence of no short-term effect.

Conclusions

Corticosteroid injections have a short-term beneficial effect on lateral epicondylitis, but a negative effect at intermediate term. Evidence on long-term effect is conflicting. Manipulation and exercise and exercise and stretching have a short-term effect, the latter also a long-term effect.

Trial registration

None.

Article summary

Article focus

- What is the current evidence for the effect of treating lateral epicondylitis with corticosteroid injection or non-electrotherapeutic physiotherapy compared to control?

Key Messages

- Corticosteroid injections have a short-term beneficial effect on lateral epicondylitis, but a negative effect at intermediate term. Evidence on long-term effect is conflicting.
- There is evidence for a short-term effect of manipulation and exercise and exercise and stretching, for the latter also on long-term.

Strengths and limitations of this review

- We found overall few good quality studies on these treatments, making a meta-analysis possible only for a few studies and outcomes.

Introduction

Lateral epicondylitis of the elbow is a frequently encountered complaint in general practice with an incidence of 4 - 7 per 1000 per year [1-3]. It is characterised by pain and tenderness over the lateral humeral epicondyle and pain on resisted dorsiflexion and radial deviation of the wrist. It is usually a self-limiting condition, often resolving in 6 to 12 months regardless of treatment, but complaints may last up to 2 years or longer [4]. Due to considerable pain and discomfort, many patients need time off from work.

Most authors attribute the condition to a lesion in the short radial extensor muscle [1, 5]. A recent study has found evidence of reduced hyperaemia measured with spectral and colour Doppler in lateral epicondylitis treated with corticosteroid injection, suggesting evidence of an inflammatory component [6]. Others, finding little evidence of inflammation have proposed the term "lateral epicondylalgia" for the condition [7].

Most patients with lateral epicondylitis are treated in general practice, and although a large number of treatments are in use, there is no consensus on which treatments are most effective. The Cochrane Library has reviewed several treatments. For topical NSAIDs and NSAIDs taken orally, the conclusion is that both may have a short term effect [8]. For extracorporeal shockwave therapy, a review of nine studies including 1000 patients found this treatment to have no effect [9]. For acupuncture [10], deep friction massage [11], orthosis [12] and surgery [13] the reviews were inconclusive due to few and methodologically weak studies.

Four review articles have been published on the effect of corticosteroid injections [14-17]. They found a short-term effect of corticosteroid injection, but no proven long-term effect, and one review found evidence of a negative long-term effect [15]. However, some of the reviews included non-controlled studies [14, 16] and non-randomised studies [16]. In one

review [15], four of 12 included studies had no control group and one was a small pilot study with short follow up. Based on this, we find the evidence in published reviews on the long-term effect of corticosteroid injections to be conflicting.

Five reviews of physiotherapeutic interventions show that there are few published studies on the effect of non-electrotherapeutic treatment, and many have methodological weaknesses [16, 18-21]. Bisset et al. [18] found evidence that manipulation and exercise had a short term effect. Four other reviews [16, 19-21] found short-term effects of mobilisation, manipulation and exercise. Three of these reviews included non-randomised or non-controlled studies [16, 19, 21]. Most previous systematic reviews have included electrotherapeutic physiotherapy such as ultrasound and extra-corporeal shockwave [14, 16, 20, 21].

Since there is no established, well-documented treatment to which new treatments can be compared, the use of a control group is important. The natural course of the condition, where most patients eventually recover regardless of intervention, makes this even more necessary. In a comparison of two different treatments, any effect found may only reflect this natural course of recovery unless the treatments prove better than a control group with no treatment.

It has been shown that systematic reviews which include studies with low scores on internal validity may over-estimate effect sizes, thus introducing a potential bias to the review [22]. There may also be a problem using rating scales with heterogeneous criteria, including i.e. criteria related to external validity, interpretation or ethical issues [22, 23].

To address these issues, a new systematic review on non-electrotherapeutic physiotherapy and corticosteroid injection seemed warranted. We wanted to include only randomised studies with a control group with no treatment or studies in which the groups only differed in regards to the investigated treatment. An established quality rating scale would be

used. We also wanted to review the most current evidence on the efficacy of corticosteroid injection, since previous reviews have differing conclusions on long-term effect.

Objective

The aim of this review was to assess the current evidence for the efficacy of corticosteroid injection and non-electrotherapeutical physiotherapy compared with control in patients with tennis elbow.

Methods

We followed the recommendations of the Cochrane Collaboration [24] and the PRISMA Group [25] in the search and report of this systematic review.

Study selection

We used the following inclusion criteria:

Study type

Randomized, controlled trials assessing treatments for lateral epicondylitis or tennis elbow were eligible for inclusion. The studies had to have at least one treatment group and one control group. We defined a control group as a group receiving no treatment (a wait-and-see approach), common treatments with expected or known moderate effect (advice, rest, NSAIDs, pain-killers) or the same treatment as the experimental group with the exception of the investigated treatment.

Participants

All age groups with a clinical diagnosis of lateral epicondylitis were included without restriction on gender.

Treatments

We searched for studies investigating or comparing the efficacy of one of the following treatments: corticosteroid injection, non-electrotherapeutic physiotherapy including stretching, mobilisation, manipulation, massage, exercise or home training. Studies on splinting, ultrasound, shock wave and other electrotherapeutic modalities were excluded.

Outcome measures and follow up

At least one validated, patient-centred outcome was necessary. This could include outcomes important to the patient such as pain, range of movement, grip strength, work status and relevant functional questionnaires. We included only studies done in a clinical setting with at least four-week follow-up of treatment effect.

Study quality assessment

We used the 11-item PEDro scale to assess the quality of the studies included in the review. This rating system closely resembles the Cochrane Collaboration Scoring system [24] and is based on the Delphi list, developed for quality assessment of randomised controlled trials by Verhagen et al. [26]. It has been used in several previously published reviews [15, 18, 19]. The PEDro scale assesses the internal and external validity of a study by addressing the issues of eligibility criteria, randomisation, allocation, blinding, statistics and data reporting. The reliability of this scale has been confirmed by Maher et al in 2003 [27]. The maximum score is 10, since item number one on the scale (specified eligibility criteria) is not counted.

A minimum score of 5 out of 10 points (50%) was chosen to be necessary for inclusion in the review, as inclusion of lower quality studies in a systematic review may over-estimate the treatment effect of interventions [28]. Ten studies were independently assessed

by two researchers (MO, ØH) [29-38] and three studies were rated by both researchers together [39-41]. The final decision on PEDro score was reached by consensus.

Search methods for identification of studies

Electronic searches

From October 2009 to January 2010, we searched the following databases for publications: Medline (Ovid and PubMed), EVSCO/Cinahl, Embase, Allied and Complimentary Medicine, The Physiotherapy Evidence Database (PEDro) and the Cochrane RCT register. The searches within each database were done without restrictions on dates or languages. We used free text, not MESH terms, in these searches, and the key terms used were ”tennis elbow”, ”lateral epicondylitis”, epicondylalgia, elbow, randomised, randomized, injection, corticosteroid, and physiotherapy. The Boolean operator AND was used to link diagnostic terms and treatment where applicable. An additional search was done in September 2012 to identify any recently published studies.

Searching other resources

Further search was done in the reference list of articles initially considered for review.

Selection of studies

The searches resulted in a number of studies potentially eligible for inclusion. Titles and abstracts were then read by two researchers independently (MO, ØH) and potential studies were selected based on the inclusion criteria. The final decision on inclusion was made by consensus from reading the full-text documents.

Data extraction and statistical analysis

The included studies were read in full text and assessed by two independent researchers (MO, ØH). One article, published in Italian, was translated by a professional bureau [41]. A

standardized set of data was extracted from each selected study and recorded using standardized forms. We calculated statistics using the statistical computing language R (www.r-project.org, The R Foundation for Statistical Computing, Vienna, Austria). We reported the results of the outcome measures for three different timings of follow-up, defined as short-term (four to 12 weeks after randomisation), intermediate term (six months after randomisation) and long-term (more than six months after randomisation). For dichotomous data, we calculated relative risk (RR) and 95% confidence intervals (CI) with the R-project library "epi.R", for continuous data the standardised mean difference (SMD) and 95% CI with the R-project library "compute.es". We pooled estimates when we found sufficient clinical and statistical homogeneity between trials using the I^2 statistic, defined as I^2 less than 65% [42].

Some studies did not report the mean, standard deviation or number of samples, which were necessary to calculate SMD. Additional calculations were then required. For Coombes [38], the median and the interquartile range (IQR) were given. We set the median as the mean value and the standard deviation was given by IQR/1.35 under the assumption of normal distribution. For Newcomer [33], the standard deviation was calculated by t-statistics obtained by the p-value and degrees of freedom. For Price [34], the t-statistics was obtained by the degrees of freedom and 95% probability. The standard deviation was estimated by the t-statistics, the mean value and upper/lower confidence intervals.

For overall improvement, a RR larger than 1 favoured treatment, and was statistically significant if the CI excluded 1. We defined the effect as large for values larger than 2 or less than 0.5, medium between 0.5 and 0.8 and between 1.25 and 2 and small for values between 0.8 and 1.0 and between 1.0 and 1.25.

For continuous data, a positive or negative SMD favoured treatment depending on the outcome measures, ie. for pain a negative SMD favoured treatment and for grip strength a

positive SMD favoured treatment. SMD was statistically significant if the CI excluded zero. We defined the effect as large for SMD more than 0.8, medium between 0.5 and 0.8 and small for values less than 0.5. For outcomes that could not be pooled, we graded the strength of the scientific evidence as strong (consistent findings in several high-quality randomised controlled studies), moderate (one high-quality randomised controlled study), conflicting (inconsistent finding between many studies) or no evidence [43].

Inter-rater reliability

The inter-rater reliability for the individual PEDro scores was assessed by calculating the intra-class correlation coefficient [44]. The R-project library "psych" was used for this calculation. A substantial inter-rater reliability was found (intra-class correlation coefficient 0.69 (0.15-0.91), $p<0.01$).

Results

The search retrieved an initial 839 hits, representing 640 individual articles. The further selection process is outlined in Figure 1. 623 articles were excluded based on title and abstract in a preliminary review. 17 articles [29-37, 39, 41, 45-50] were then assessed using the full-text documents. Three were found not to be randomised controlled trials [45-47], two had a PEDro quality rating below 50% (Table 2) [37, 39] and three had a follow-up shorter than four weeks [48-50]. The additional search done in september 2012 retrieved two possible studies [40, 51], one of which was excluded for not having a control group [51]. A recently published study was also assessed [38] and a total of 11 studies were included in the final review [29-36, 38, 40, 41].

Included studies

The characteristics and details of each study are given in Table 1. The included studies represented a total population of 1161 patients. Several studies had more than one treatment

group, so the 11 included studies investigated 15 treatment groups relevant for this review. For the statistical analysis, one study which used two different corticosteroids, was treated as two studies [34].

The mean age of patients varied from 41 to 51 years and the female percentages varied from 35 to 63. There were large differences in duration of complaints at baseline between studies. Most had a duration of several weeks to months and only one stated a short duration [33]. Eight studies had control groups with no active treatment [29-31, 34-36, 38, 40], e.g. a wait-and-see group or NSAIDs. Two of these used lidocaine as a placebo injection [31, 34]. In the three other studies, the control and treatment groups both received similar active treatments, with the intervention group in addition receiving the treatment to be investigated [32, 33, 41] .

Eight studies investigated corticosteroid injections, representing 925 patients [29-31, 33-36, 38]. Five different corticosteroids were used, with different dosages and injection techniques. The control groups received no active treatment in seven of the eight studies, in one study both the control and treatment group received additional exercise treatment [33]. Seven of the studies had a long-time follow up of 24 weeks or more [29-31, 33-35, 38].

There were few studies covering non-electrotherapeutic physiotherapy. We found five studies which could be included, representing 600 patients [29, 32, 38, 40, 41]. The treatment modalities investigated were manipulation and exercise [29, 38], concentric or eccentric exercises [32], exercise [40] and eccentric exercises with stretching [41]. Three studies had a control group with no active treatment [29, 38, 40], the other two had control groups that received stretching and orthosis respectively. Three studies [29, 38, 41] had a follow up of 24 weeks or more.

The most frequently used outcome measures were assessment of pain and grip strength. Six studies measured pain free grip strength with handheld dynamometers [29-33,

35]. Eight studies used a number of different questionnaires covering pain, function and disability [29-33, 35, 38, 40]. Nine studies assessed pain on a visual analogue scale or Likert-scale [29-34, 36, 38, 40], and six studies rated patient's assessment of improvement on graded scales [29, 30, 35, 36, 38, 41].

Risk of bias in included studies

We addressed the issues of the quality of the included studies and completeness of reported data by rating them with the PEDro scale (Table 2). Most studies used a computerized randomisation schedule, and seven of the eleven studies used concealed allocation [29-31, 35, 38, 40, 41]. Baseline comparison was done in all studies, the dropout rate was below 15% in ten studies [29, 30, 32-36, 38, 40, 41] and intention to treat analysis was stated in all studies. There was between-group analysis of at least one outcome measure in all the studies, and both point-measures and variations of outcome measures were reported in all studies.

The use of blinding was more diverse among the studies. Blinding the subject for treatment is difficult for physiotherapeutic treatments, but the use of blinded assessors reduces the risk of bias. None of the studies on physiotherapy in our review had blinded subjects or therapists, but two used blinded assessors [29, 38]. This might give biased results in the studies covering physiotherapeutic treatments.

For the eight studies on corticosteroid injection, the number using blinding was larger. There was blinding of subjects in four studies [31, 33, 34, 38], of the treating doctor in two [31, 33] and of assessors in six studies [29-31, 34, 35, 38].

In several studies the control group received some form of treatment (although similar to the treatment group) [32-34, 36, 41]. In these studies, synergistic effects between the treatments cannot be ruled out. This makes the results more difficult to interpret. Two studies had a short follow up of four and six weeks [32, 36], which for a condition usually lasting

several months, reduces the clinical implication of the results. Difference in duration of complaints at baseline also complicates comparison between studies.

Effects of interventions

Corticosteroid injection

The efficacy of corticosteroid injection for treating lateral epicondylitis was investigated in eight studies (Table 3 and Figure 2 [52]). For short-term follow up, heterogeneity between studies made pooling of outcomes only possible for pain. For corticosteroid injection vs no intervention or NSAIDs, we found strong evidence for a beneficial effect on overall improvement and a large positive effect on pain [29, 30, 35, 36, 38]. For grip strength, we found moderate evidence for a negative effect [35]. For corticosteroid injection vs lidocaine injection, evidence was conflicting for effect on pain, with two studies showing a large positive effect (Price et al. using hydrocortisone and triamcinolone) [34] and one showing no significant difference [31]. For maximum grip strength, the evidence was also conflicting, with one study showing a large postitive effect of treatment (Price et al. using triamcinolone)[34], and two studies showing no statistical difference (Lindenhovius, Price et al. using hydrocortisone) [31, 34]. For corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found moderate evidence for no significant difference on pain and grip strength [33].

At intermediate follow-up, we found sufficient homogeneity to poole estimates for overall improvement [29, 30, 38] and pain [29, 30, 35, 38] for corticosteroid injection vs. no intervention or NSAIDs. For overall improvement this showed a medium negative effect and for pain a small negative effect. For maximum grip strength, pooling of corticosteroid injection vs no intervention, NSAIDS and lidocaine showed a small negative effect [31, 34, 35]. For corticosteroid injection vs lidocaine injection, pooling of estimates was not possible due to heterogeneity. For pain, two studies showed a large negative effect (Price et al. using

hydrocortisone and triamcinolone)[34], and one study showed no significant difference [31], thus the evidence was conflicting. For grip strength, the evidence was also conflicting, with the same two studies showing a large negative effect [34] and one showing no significant difference [31]. For corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found moderate evidence of no significant effect on pain [33].

At long-term follow-up, pooled estimates of overall improvement showed no difference in effect of corticosteroid injection vs no intervention or NSAIDs [29, 30, 35, 38]. For pain, heterogeneity prevented pooling and we found the evidence conflicting with one study showing a large negative effect [30], and three others showing no significant difference in effect [29, 35, 38]. For grip strength, we found moderate evidence of no significant difference [35]. For corticosteroid injection vs lidocaine injection and corticosteroid injection, exercise and stretching vs exercise and stretching alone, we found no data on long-term effect.

Physiotherapy

We included five studies (n=600) investigating non-electrotherapeutical physiotherapy, representing five different treatment modalities (Table 4 and Figure 3 [52]).

Two studies investigated the efficacy of manipulation and exercise vs. no intervention [29, 38]. At short-term, pooled estimates showed a large positive effect on overall improvement. For pain, pooling was not possible due to heterogeneity. We found strong evidence for a beneficial effect, for pain free grip strength we found moderate evidence for a beneficial effect. At intermediate-term, pooled estimates showed no difference between treatment and control for neither pain nor overall improvement. There was moderate evidence for no difference in pain free grip strength. At long-term, pooled estimates again showed no difference between treatment and control for either pain or improvement and we found moderate evidence for no difference in pain free grip strength.

The efficacy of exercise vs no intervention was investigated in one study [40]. We found moderate evidence for no short-term difference in effect for outcomes on pain and DASH-score. There was no data on intermediate- or long-term effect.

For eccentric exercise and stretching vs stretching, investigated in one study [32], we found moderate evidence for no short-term treatment effect for outcomes on pain, pain-free grip strength and DASH-score. There was no data on intermediate- or long-term effect.

The same study also investigated the efficacy of concentric exercise and stretching vs stretching. We found moderate evidence for no short-term treatment effect for outcomes on pain, pain-free grip strength and DASH-score. There was no data on intermediate- or long-term effect.

Eccentric exercise and stretching vs no intervention was investigated in one study [41]. We found moderate evidence for a positive effect on pain and grip strength at short-term follow up. There was no data on efficacy at intermediate follow-up, but at long-term, we found moderate evidence of a positive effect on overall improvement, pain and grip strength.

Discussion

Summary of main results

This review found overall evidence for a short-term beneficial effect of corticosteroid injection. At intermediate follow-up, the evidence showed an overall negative effect. For corticosteroid injection vs lidocaine injection, we found the evidence to be conflicting. At long-term follow up, the evidence suggest no difference in effect on overall improvement and grip strength, but the evidence was conflicting for pain. For manipulation and exercise vs no intervention, we found an overall beneficial effect at short term, but no significant difference at intermediate or long-term follow-up. The evidence on exercise vs no intervention showed no differences at short-term follow up. For eccentric exercise and stretching vs stretching

alone, the evidence showed no short-term difference in effect. The same was found for concentric exercise and stretching vs stretching. The evidence on eccentric exercise and stretching vs no intervention showed a beneficial effect at short-term and long-term, while there was no data on intermediate follow-up.

For treating lateral epicondylitis, this review showed evidence for a short-term benefit of corticosteroid injection and manipulation with exercise. Eccentric exercise and stretching showed beneficial effect both at short- and long-term follow-up.

Overall completeness and quality of the evidence

There is a paucity of well-designed studies for determining the effect of non-electrotherapeutic physiotherapy. The conclusions on the effect of these treatments are therefore limited. A comparison and review of several individual studies was only possible for one treatment modality, manipulation and exercise vs no intervention (Table 4).

We included eight studies treating a total of 925 patients with corticosteroid injections in our review. The conclusions for this treatment are more solid due to the larger number of studies, seven of which had long-term follow up. Due to differences in type of corticosteroids used, treatment regimes and outcome measures in the included studies, pooling of outcome measures was difficult. We found statistical heterogeneity for most outcomes, and pooling was only possible for a few of the outcomes and follow-ups. The long-term effect of corticosteroid injection showed conflicting results in the included studies. The large differences across the studies in duration of complaints at baseline, corticosteroids used in different dosages, and control group treatments may explain this.

The difference in duration of complaints at baseline complicates the interpretation and comparison of the results, since there might be different effects of the treatments on an epicondylitis of recent onset compared to one that has lasted several months. This is also reflected by Cook [53] who considered tendinopathy as a continuum with three stages and

different characteristics and presumably treatments for each stage. Haahr [54] found that high physical strain at work, work with manual tasks, high perceived stress at baseline and a high level of pain and dysfunction seem to predict an unfavourable outcome after one year. Thus any differences in baseline characteristic for these parameters might possibly influence between-group differences of outcome.

Potential biases in the review process

The search process, selection of search terms and possible errors in reading and assessing the large number of articles represent a possible bias. Although we have searched several databases with a number of search terms, we may have missed some published studies. To reduce the risk of bias in the inclusion process, we used two reviewers who independently screened articles.

Our choice of inclusion criteria, especially the type of control or comparison treatment and the use of a cut-off quality score (PEDro), has important implications for the conclusions that can be drawn from this review. The efficacy of the treatments are here only compared with a control (no treatment) or to an underlying treatment that is common to both intervention groups, so no conclusion can be drawn on which of two different treatments is best.

To address the issue of publication bias, we searched two clinical trial registries: ClinicalTrial.gov (US National Institutes of Health) and Current Clinical Trials. We found no completed, unpublished studies on corticosteroid injection. Two completed studies on non-electrotherapeutic physiotherapy were found. One from The United Kingdom completed in 2008 on manipulation with movement and one from Sweden completed in 2009 on eccentric training. We have found no published articles from these studies. Unpublished studies are not indexed in PubMed or other databases and older studies may have been conducted without

registration in a clinical trial registry, making it difficult to make an overall assessment of publication bias.

Agreements and disagreements with other reviews

Our findings agree with earlier reviews [14, 16, 17, 55]. We found consistent evidence of a beneficial short-term effect of corticosteroid injections, but evidence on the long-term effect is still conflicting. Coombes et al. [15] found in their review that corticosteroid injections have a worse outcome in the long term than most conservative interventions for tendinopathies of different locations. The included studies in our review did not allow for a similar strong conclusion on the long-term effect of corticosteroid injections. For non-electrotherapeutical physiotherapy, we agree with earlier reviews [14, 16, 18, 19, 21] that there is moderate evidence of a short-term effect of manipulation and exercise. Our review strengthens this conclusion with the inclusion of a recently published study [40]. In addition, we found moderate evidence of both short- and long-term beneficial effect of eccentric exercise and stretching.

Authors' conclusions

Implications for practice

We found that both corticosteroid injection and manipulation with exercise gave a short-term benefit compared to control for treating lateral epicondylitis. At intermediate term, treatment with corticosteroid injection came out worse, while manipulation with exercise was not different from control. At long term, both treatments showed no benefit over control. For patients wanting treatment, it seems reasonable to recommend manipulation and exercise. For patients with mild symptoms, a wait-and-see approach would be appropriate. Though showing a large short-term benefit, the negative intermediate-term effect and uncertain long-term effect of corticosteroid injection make this treatment difficult to recommend. Eccentric

exercise with stretching showed efficacy both on short- and long-term follow-up, but only in one study.

Implications for research

We found few studies and some conflicting results on the long-term efficacy of corticosteroid injection. More trials or a meta-analysis with individual patient data from earlier studies might give better answers to the question on long-term effect.

For non-electrotherapeutical physiotherapy, more studies with a randomised, controlled design are needed. Blinding, for example by using a blinded assessor, should be applied wherever possible. The promising results of manipulation with exercise and eccentric exercise with stretching need further investigating.

Future studies should differentiate between acute and chronic complaints. Baseline levels of perceived pain, stress levels, handedness and presence of physical stress at work should be recorded. Standardization in the usage of outcome measures will enable data pooling and meta-analyses in future reviews. Studies investigating the combined effect of physiotherapy and corticosteroid injection treatments would also be useful. Most patients with acute lateral epicondylitis are treated in a general practice setting, and future research should be performed in such a setting.

Acknowledgements

Morten Olaussen and Oeystein Holmedal designed the study, performed the searches, read articles, decided which articles to include, performed the data extractions, interpreted the findings and wrote the main manuscript. Morten Lindbaek designed the study, decided which articles to include, interpreted the findings and revised the manuscript. Soeren Brage decided which articles to include, interpreted the findings and revised the manuscript. Hiroko Solvang

did the statistical calculations and analysis, interpreted the findings and revised the manuscript.

Competing interests

The authors declare that they have no competing interests.

Funding

Our work was funded by The Fund for General Practice Research, The Norwegian Medical Association, Oslo, Norway.

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FIGURES AND TABLES

uploaded as web only data:

Table 1: Demographics, treatments and outcome measures in the ten included studies

Table 2: Quality rating of included studies by assessing internal and external validity with the PEDro scale

Table 3: Effect size of improvement rate, reduction in pain and increase in grip strength for corticosteroid injection

Table 4: Effect size of treatment effects for non-electrotherapeutic physiotherapy

Figure 1: Outline of the selection process

Figure 2: Forest-plot of effect sizes for corticosteroid injection

Figure 3: Forest-plot of effect sizes for non-electrotherapeutic physiotherapy