Corticosteroid injections for lateral epicondylitis: a systematic overview

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SUMMARY

Background. *Lateral epicondylitis (tennis elbow) is a common complaint, for which corticosteriod injections are a frequently applied therapy. However, there were no up-to date reviews available that systematically addressed the effectiveness and adverse effects, including questions concerning optimal timing of injections and composition of the injection fluid.*

Aim. *The aim of the study was to assess the effectiveness of corticosteroid injections in the treatment of lateral epicondylitis (tennis elbow) by systematic review of the available randomized clinical trials.*

Data sources. *The data sources used were randomized clinical trials identified by literature searches of the MedLine (1966–1994) and Embase (Exerpta Medica) (1980–1994) databases for the keywords epicondylitis, tendinitis and elbow, injection. References given in relevant publications were further examined.*

Study selection. *The criteria for selecting studies were as follows: randomized clinical trials (treatment allocation in random or alternate order); one of the treatments to include one or more corticosteroid injections (additional interventions were allowed); participants suffering from lateral epicondylitis; and publication in English, German or Dutch. Abstracts and unpublished studies were not included.*

Data synthesis. *Methodological quality was assessed by means of a standardized criteria list (range 1–100 points). The extracted outcomes were the general conclusion drawn by the authors of the reports on the trials, and the success rates at the various follow-up points as (re)calculated by us. The success rates were subsequently graphically displayed and statistically pooled. Separate stratified analyses were conducted according to a predetermined analysis plan.*

Results. *Twelve randomized clinical trials were identified. The median methodological score was 40 points, indicating an overall poor to moderate quality. The pooled analysis indicated short-term effectiveness (2–6 weeks): pooled odds ratio (OR) = 0.15 [95% confidence interval (CI) 0.10–0.23], χ^2 [degrees of freedom (df = 5) = 13.3], indicating statistical heterogeneity. At longer term follow-up, no difference could be detected. The studies of better methodological quality indicated more favourable results than those of lesser methodological quality. The most suitable corticosteroid to use as well as dosage, injection interval and injection volume could not be derived from the various trials.*

Conclusion. *The existing evidence on corticosteroid injections for the treatment of tennis elbow is not conclusive. Many trials were conducted in a secondary care setting and clearly had serious methodological flaws, and there was statistical heterogeneity among the trials. Corticosteroid injections appear to be relatively safe and seem to be effective in the short term (2–6 weeks). Although the treatment seems to be suitable for application in general practice, further trials in this setting are needed. As yet, questions regarding the optimal timing, dosage, injection technique and injection volume remain unanswered.*

Keywords: tennis elbow; meta-analysis; corticosteroid injections; therapy.

Introduction

LATERAL epicondylitis (tennis elbow) is a common complaint causing characteristic pain and sensitivity in the lateral elbow region. In contrast to what is widely thought, only a small proportion (5%) of cases are actually caused by playing a racket sport. The ailment has an incidence of 4–7 per 1000 per year in general practice, with a peak between the ages of 35 and 54 years.[1-3] The duration of an average episode is estimated to be between 6 months and 2 years.[4] In the Netherlands, 10–30% of all episodes of tennis elbow result in absence from work, with an average duration of 12 weeks,[2,5,6] resulting in a high loss of productivity. There is a great variety of potential therapies, surgical intervention being the most radical. In general practice in the Netherlands, pain-relieving medication (18–35%), corticosteroid injections (14–38%) and physical therapy (28–30%) are the most frequently applied therapies.[2,3]

Compared with physical therapy, corticosteroid injections have some clear advantages for the general practitioner: injections are easy to administer, referral is not necessary and the treatment is relatively cheap. There is little consensus on the optimum timing of corticosteroid injections. Some experts advocate injections when the patient does not respond to a certain period of rest,[7] whereas others argue that injectable steroids should be deferred as long as possible.[8] In addition, disagreement exists about which substance to use, the need to include a local anaesthetic and the total volume to be injected.[9] Estimates of the risk of adverse effects also vary considerably.[10]

In general, reviewers consider corticosteroid injections to be an effective treatment for tennis elbow.[9,11] However, in a recent review, Labelle *et al*[12] evaluated five randomized clinical trials (RCTs) on the effectiveness of corticosteroid injections for this complaint. They argued that the methodological quality of the available RCTs was low, and therefore, refrained from statistical pooling. It was concluded that there was insufficient scientific evidence to support the use of corticosteroid injections.

The review by Labelle *et al*[12] only covered the RCTs indexed in MedLine during a limited period (1966–90), thereby neglecting non-indexed RCTs and RCTs published before 1966 and after 1990. Refraining from pooling the data, as they did, is only one of the available options when dealing with the insufficient

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methodological quality of RCTs. There are other ways of weighing quality scores in the meta-analysis of RCTs.[13] Thus, we decided to perform a new, more comprehensive, systematic review. We have systematically assessed the evidence from all available, published RCTs in order to determine the current state of the art regarding the effectiveness of corticosteroid injections. In our review, we also emphasize the methodological quality of the studies, as even RCTs may show biased outcomes related to methodological shortcomings in the design, execution and reporting.[14] Furthermore, we incorporate statistical pooling of the results according to a predetermined analysis plan.

Method

Selection of studies

A literature search of Medline was carried out for the period 1966–1994 and of Embase (Exerpta Medica) for the period 1980–1994. Subject headings and keywords used were *epicondylitis, tendinitis* and *elbow, injection.* A number of pharmaceutical companies were contacted and provided results from their in-house databases of published studies. In addition, the references given in relevant publications were also examined. Abstracts and unpublished studies were not included. All studies had to meet the following criteria:

1. They had to be in the form of a randomized clinical trial (treatment allocation in random or alternate order).
2. One of the treatments had to include one or more corticosteroid injections (additional interventions were allowed).
3. The subjects participating in the trial had to suffer from lateral epicondylitis.
4. The publications were to be written in English, German or Dutch.

Table 1. Criteria list for the methodological assessment of randomized clinical trials of corticosteroid injections for lateral epicondylitis (for details, see Appendix 1).

Criterion	Weight
Study population	
A Selection and homogeneity	4
B Randomized procedure adequate	3
C Prognostic comparability	7
D Handling of drop-outs	3
E < 20% loss to follow up	1
< 10% loss to follow up	3
F ⩾ 25 subjects in the smallest group	6
⩾ 50 subjects in the smallest group	9
⩾ 75 subjects in the smallest group	15
Interventions	
G Interventions included in protocol and described	10
H Placebo controlled	5
I Pragmatic study	5
J Handling of co-interventions	5
Effect	
K Blinding of patients and physician	5
L Outcome measures relevant	10
M Blinded outcome assessments	10
N Follow-up period adequate	5
Data presentation and analysis	
O Intention-to-treat analysis	5
P Frequencies of most important outcomes presented for each treatment	5

Assessment of validity

After collection of the papers, all trials were scored according to the criteria listed in Table 1 and Appendix 1. The criteria are based on generally accepted principles of intervention research.[15] Similar criteria have previously been used in review articles about physiotherapy treatment for several musculoskeletal disorders.[16,17] A weight was attached to each criterion, and the maximum score for each study was 100 points. The methodological quality of the studies was assessed independently by two reviewers (W J J A, E M H). In a subsequent meeting, the reviewers tried to reach consensus on each criterion they had initially disagreed upon. Where disagreement persisted, a third reviewer (L M B) made the final decision. The assessments resulted in a hierarchical list, in which higher scores indicate studies of higher methodological quality. The outcome of the studies will be discussed in relation to their methodological scores.

Outcome of the studies

A study was judged to be positive if the authors concluded (in their abstract or conclusions) that steroid injection therapy was more effective than the reference treatment. Usually, this meant that the difference in effect for the primary outcome measure was statistically significant at the conventional 5% level. In a negative study, the authors reported no differences between the study treatments, or more favourable results for the reference treatment. In addition to the authors' conclusion, we also extracted the data regarding the success rates at the various follow-up points. If a global measure of improvement was presented, the various categories were dichotomized into 'success' or 'failure' (see Table 3). If no categorical measure of improvement was presented, a binary outcome of 'success' or 'failure' was tried in other ways, which will be illustrated when applicable (Table 3). If the measure of improvement was reported by both an assessor and the patient, the opinion of the latter was selected. The binary outcomes were subsequently entered into a statistical meta-analysis. We used the software of the Cochrane Collaboration, the Review Manager.[18] The effects of binary data are expressed in odds ratios (ORs), fixed effects model. Confidence levels were set at 95%.

Separate stratified analyses according to a predetermined analysis plan were placebo-controlled trials versus pragmatic trials, low-quality trials versus high-quality trials, and short-term follow-up versus long-term follow-up. For analyses that did not involve different follow-up periods and for trials presenting various follow-up points, we chose the follow-up moment considered to be most important by the authors of the article.

Results

Trials included

A total of 11 articles on RCTs were identified. Six were identified in the on-line search and five as a result of additional efforts. One article included two relevant contrasts[19] and was methodologically assessed for each individual contrast. Therefore, the tables present the results for 12 trials, the trials of Price *et al*[19] being reported as Price *et al* 1991a and 1991b. Ten trials compared corticosteroid injections with another (placebo) treatment, whereas two compared different corticosteroid regimens. Of these, one compared different dosages of corticosteroids (Price *et al* 1991a)[19] and the other compared needle injection with hypospray, a high-pressure needleless insertion technique.[28] We excluded the trials of Clarke & Woodland[29] and Brattberg,[30] which were included in the review of Labelle *et al*,[12] because we could not find any plausible reference to a randomization procedure in these publications. An RCT conducted by Jonquière[31] was excluded because only two of the 32 patients receiving Cyriax treatment actually received a corticosteroid injection. One RCT evaluating an injec-

tion involving a vasoconstrictor was excluded because it did not include treatment with a corticosteroid.[32]

None of the RCTs was conducted in general practice. The only studies conducted in primary care were carried out by Halle *et al*[25] in an army clinic, and by Kivi[27] in an occupational health centre. Four studies were conducted before 1980[23,24,26,28] and four were published after 1990.[2,19,22]

Methodological score

The initial disagreement on the methodological score was 11% (60 of 46 x 12 = 552 subitems). Most of the disagreement was caused by reading and interpretation errors, and could easily be solved in a subsequent consensus meeting. Involvement of the third reviewer (L M B) for final decisions was not necessary .

The results of the methodological assessment are presented in Table 2. The scores ranged from 29 to 63, and four studies scored more than 50 points.[2,19,20] The median score was 40 points, indicating an overall poor to moderate methodological quality. The most prevalent methodological shortcomings were in the areas of (A) selection and homogeneity of the study population (which constituted only 6% of the maximum attainable score on this item for all studies together), (B) description and execution of the randomization procedure (8% of the maximum possible score), (C) (description of) prognostic comparability of the groups (27%), (F) small sample size (15%), (J) handling of co-interventions (27%), and (K) blinding of the patient and physician (23%). In addition, (L) the relevance and completeness of the outcome measurement (38%) and (M) blinded outcome assessment (38%) produced relatively low item scores.

Results of RCTs

In five out of the 10 trials presented in Table 3, corticosteroid injections plus local anaesthetic were compared either with local anaesthetic only or with normal saline.[19,21,23,24,26] The other trials were pragmatic, comparing corticosteroid injections with Cyriax physiotherapy,[2] naproxen,[20] elbow band or wrist brace,[22] naproxen and wrist brace,[27] or with ultrasound, phonophoresis or transcutaneous electrical nerve stimulation (TENS).[25] Six out of 10 trials reported positive results.[2,19,21,22,23,26] Of the five methodologically best trials, only the small trial conducted by Saartok & Eriksson[20] (n = 10 for each group) reported negative results. The positive trials reporting both short-term and long-term results[2,19,22] showed a general trend that corticosteroid injections are effective in the short term (2–6 weeks), but not after a longer follow up (> 6 weeks).

Statistical pooling

Figures 1 and 2 provide a graph of the outcomes at different follow-up points. The changes in the visual analogue pain score of Price *et al*[19] were dichotomized: ≤ 0 as 'failure' and > 0 as 'success'. No further data were available from Halle *et al*,[25] so this trial was not included, resulting in nine trials available for statis-

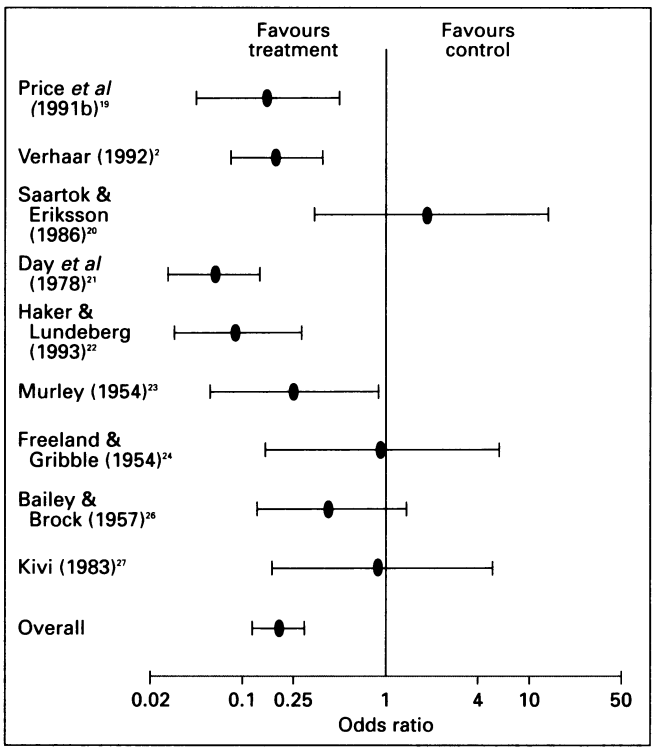

Figure 1. Effectiveness of corticosteroid injections for epicondylitis. Odds ratios for binary outcome ('treatment success') for the most important follow-up assessment according to the authors of the trials reports. Horizontal lines denote the 95% confidence intervals. Dots represent point estimates. Trials are ranked in a decreasing order of methodological quality.

Table 2. Methodological quality of randomized clinical trials evaluating the effectiveness of corticosteroid injections for lateral epicondylitis.

	Methodological criteria																Methods score	
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P		
Reference	4	3	7	3	3	15	10	5	5	5	5	10	10	5	5	5	100	Conclusion
Price *et al* (1991a)[19]	-	-	7	1	1	6	10	-	5	-	4	6	8	5	5	5	63	Equal*
Verhaar (1992)[2]	1	3	5	1	3	9	9	-	5	-	-	8	-	5	5	5	59	Positive
Price *et al* (1991b)[19]	-	-	3	1	3	6	10	5	-	-	2	6	8	5	5	5	59	Positive
Saartok & Eriksson (1986)[20]	-	-	3	3	3	-	10	5	-	5	1	8	6	3	-	5	52	Negative
Day *et al* (1978)[21]	-	1	-	3	3	6	10	5	-	-	1	2	6	-	5	5	47	Positive
Haker & Lundeberg (1992)[22]	1	-	5	-	1	-	10	-	5	5	-	4	-	5	5	5	46	Positive
Murley (1954)[23]	-	-	-	3	3	-	10	5	-	-	2	2	6	3	5	5	44	Positive
Freeland & Gribble (1954)[24]	-	-	-	3	3	-	10	5	-	-	2	2	6	-	-	5	36	Negative
Halle *et al* (1986)[25]	1	1	-	3	3	-	6	-	5	3	-	2	-	3	5	-	32	Negative
Bailey & Brock (1953)[26]	-	-	-	3	-	-	6	5	-	3	2	2	6	-	-	5	32	Positive
Kivi (1982)[27]	-	1	-	3	3	-	8	-	5	-	-	2	-	5	-	5	32	Positive
Hughes & Currey (1969)[28]	-	-	-	3	3	-	8	-	5	-	-	2	-	3	-	5	29	Equal†
Per cent score per item	6	8	27	75	81	15	89	50	50	27	23	38	38	62	58	92	44	

*Compares two dosages. †Compares two injection techniques.

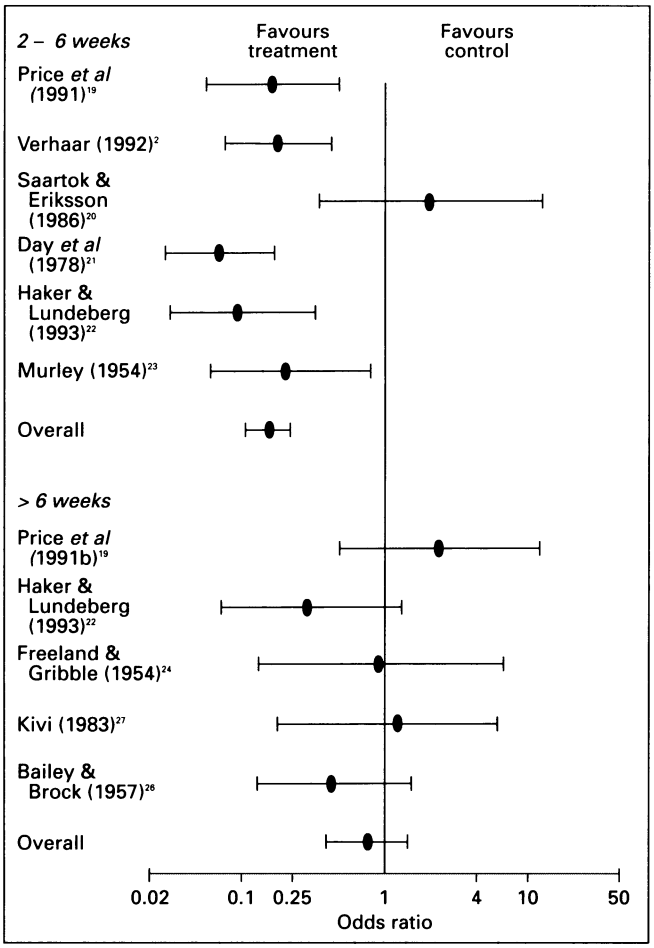

Figure 1. Effectiveness of corticosteroid injections for epicondylitis. Odds ratios for the binary outcome ('treatment success') at follow-up assessment 2–6 weeks after randomization and at follow-up more than 6 weeks after randomization. Horizontal lines denote the 95% confidence intervals. Dots represent point estimates. Trials are ranked in a decreasing order of methodological quality.

tical pooling. Statistical testing indicated heterogeneity in outcome among the RCTs included for both the short-term and long-term subsets. The pooled OR for 2–6 weeks was 0.15 (95% CI 0.10–0.23), indicating a favourable effect of corticosteroids. For a follow-up exceeding 6 weeks, the OR was 0.73 (95% CI 0.37–1.44), indicating a lack of a long-term effect. Verhaar[2] reported no difference between treatment groups at 52 weeks, but the data were not presented, and therefore, could not be included in this analysis.

Sensitivity analysis, stratified for methodological quality, showed an OR = 0.14 (95% CI 0.09–0.23) for the five methodologically best studies and an OR = 0.49 (95% CI 0.24–1.02) for the four methodologically worst studies. The 'placebo-controlled' studies (local anaesthetic or saline injection) gave an OR = 0.20 (95% CI 0.12–0.35) and the pragmatic studies also gave an OR = 0.20 (95% CI 0.11–0.36). Statistical testing for both sensitity analyses also indicated heterogeneity within the sub-sets.

Table 4 compares the various treatment regimes with corticosteroids. Price *et al* (1991a)[19] compared 10 and 20 mg triamcinolone and found no difference in effect. In their trial, Hughes & Currey[28] found that hypospray, a high-pressure, needleless injecting device, was just as effective as a single injection with a needle. However, the methodological score of this trial was low.

A variety of volumes and compositions of injected substances were used in the trials (Table 3). Of the corticosteroid preparations used, only triamcinolone gave positive results in several RCTs of higher methodological quality.[2,19,22] The volume injected varied from 0.5 to 2 ml, and in one RCT, it was even 3 ml.[26] The number of injections also varied: one to three injections were given. The RCTs involving more than one injection usually reported positive results.[2,19,21,22]

Adverse effects

Six RCTs explicitly reported adverse effects. Murley,[23] Saartok & Eriksson[20] and Verhaar[2] stated that no adverse effects were found. Bailey & Brock[26] described a worsening of the pain 24–48 h after the injection in 25% of the patients. This percentage was the same in patients injected with a local anaesthetic only, and in patients receiving a combination of a corticosteroid and local anaesthetic. Haker & Lundeberg[22] reported worsening of the pain for some days after injection with a corticosteroid–local anaesthetic combination in two out of the 19 patients injected. Price *et al*[19] provided the most extensive report on adverse effects. Post-injection pain was reported by 58 out of the 116 (50%) patients injected with a corticosteroid plus local anaesthetic, compared with nine out of the 29 (31%) patients injected with a local anaesthetic alone. Skin atrophy was reported in 31 out of the 116 patients (27%) treated with a corticosteroid injection compared with five out of the 29 patients (17%) injected with a local anaesthetic only. For the various corticosteroid compositions the prevalence of skin atrophy was six out of 29 (21%) for hydrocortisone 25 mg, 17 out of 57 (30%) for triamcinolone acetate (TCA) 10 mg and 8 out of 40 (20%) for TCA 20 mg.

Discussion

Methodological score

The RCTs included in this review were of only moderate methodological quality, as demonstrated by the median methodological score of 40 points. This score is similar to the scores in several methodological overviews of studies on the effectiveness of physiotherapy for musculoskeletal disorders reported previously.[16,17] The choice of items and the weighting of the items in the assessment of methodological quality are prone to subjective preferences. The choice of the items for our list is based on generally accepted principles of intervention research and covers several dimensions of methodological quality.[15] At present, there is no empirically developed, validated list available for methodological assessment of RCTs.[15] In addition to the choice of items, the process of weighting the items provides even more variation. Thus, we also performed an alternative (sensitivity) analysis, applying equal weights to all items. Using this procedure the ranking of the 'better' reviews was almost identical (data not shown).

Poor methodological quality may lead to bias, but the direction of such bias remains uncertain. On the one hand, low-quality trials might overestimate the effectiveness of the intervention, an example being the so-called expectancy bias in insufficiently blinded trials. On the other hand, low quality may also lead to less precise or biased estimates of the effects of the intervention, providing 'false-negative results'.[33] Although there is no clear reason why higher methodological quality was related to a positive outcome in our review, the identification of such a positive relationship generally supports the conclusions of a review. However, because of the low overall methodological quality of the trials, the indication that higher methodological scores were related to a positive outcome should still be interpreted with caution.

Study quality

The methodological problems encountered in trials evaluating

Table 3. Randomized clinical trials evaluating the effectiveness of corticosteroid injections for epicondylitis.

Reference	Review score	Setting	Corticosteroid injection(s) (number of patients available for follow-up)	Control treatment (number of patients available for follow-up)	Follow-up duration	Determination of success rate	Authors' conclusion	Results
Verhaar (1992)[2]	59	OPD	I TC 1% + lidocaine 1% 2ml; 1 – 3 injections (51)	II Cyriax physiotherapy 12 treatments in 4 weeks (52)	6,52 weeks	Assessor's overall rating rating four-point ordinal scale	6 weeks: positive; 52 weeks: negative	Results of corticosteroid injections at 6 weeks superior to Cyriax physiotherapy; at 52 weeks, no significant differences. SR — 6 weeks: (I) 69%, (II) 25%. SR — 52 weeks, not reported
Price *et al* (1991b)[19]	59	OPD	I TC 10 mg + lignocaine 1% 2ml; 1–2 injections (30) II HC 25 mg + lignocaine 1% 2 ml; 1–2 injections (29)	III Lignocaine 1% 2ml; 1–2 injections (29)	4, 8, 24 weeks	Patient: VAS pain* 10 mm	4, 8, weeks: positive; 24 weeks: negative	Response both steroids (I and II) significantly better up to 8 weeks, but improvement equal for all groups at 24 weeks. VAS pain* at 4 weeks: (I)17 mm, (II) 28 mm, (III) 46 mm; VAS pain* at 8 weeks: (I) 20 mm, (II) 30 mm, (III) 35 mm, VAS pain* at 24 weeks: (I) 18 mm, (II) 24 mm, (III) 12 mm
Saartok & Friksson (1986)[20]	52	OPD	I Single injection of BM (short + long-acting) 1 ml + 0.5 ml pilocaine 1% + placebo capsules 2 dd (10)	II Single injection of saline 1.5 ml + naproxen 2 dd 250 mg (10)	2 weeks	Patient's global assessment on seven-point ordinal scale: cured or markedly improved	Negative	Naproxen as effective as single injection of corticosteroid. SR: (I) 30%, (II) 40%
Day *et al.* (1978)[21]	47	OPD	I Methyl-prednisone acetate 1 ml; one or more injections (36)	II Xylocaine 1% 1 ml; one or more injections (35) III saline 0.9% 1 ml; one or more injections (29)	unclear: until cured or change of therapy	Assessor's global assessment on four-point ordinal scale: cured or improved	Positive	Corticosteroid significantly better than sylocaine or saline solution. SR: (I) 92%, (II) 20%, (III) 24%
Haker & Lundeberg (1993)[22]	46	OPD	I Bupivacaine 0.3 ml + TC 0.2 ml = 2 mg, repeated after 1 week if necessary (19)	II Elbow band (18) III Wrist splint (19)	2 weeks, 3, 6, 12 months	Patient's global assessment on five-point ordinal scale: good or excellent	2 weeks: positive; 3, 6, 12 months: negative	In subjective as well as objective outcome at 2 weeks a significant difference between the groups; later no difference; SR — 2 weeks: (I) 68%, (II) 6%, (III) 11%. SR — 3 months: (I) 67%, (II) 50%, (III) 21% (worst case analysis)
Murley (1954)[23]	44	OPD	I HC 1 ml = 25 mg (19)	II Procaine 2% 1 ml (18)	1 — 4 weeks	Assessor's global assessment on three-point ordinal scale: improved	Positive	No significance testing performed; SR — 1 week: (I) 74%, (II) 39%; SR — 4 weeks: (I) 84%, (II) 50%
Freeland & Gribble (1953)[24]	36	OPD	I Single injection of HC 1 ml = 25 mg (9)	II Single injection of procaine 5% 1 ml (7)	2–4 months	Assessor: overall improvement on signs and symptoms, pain on wrist extension and gripping	Negative	No significance testing performed; SR: (I) 44%, (II) 42%

Table 3. (Continued)

Reference	Review score	Setting	Corticosteroid injection(s) (number of patients available for follow-up)	Control treatment (number of patients available for follow-up)	Follow-up duration	Determination of success rate	Authors' conclusion	Results
Bailey & Brock (1957)[26]	32	OPD	I Single injection of 1 ml (=25 mg) HC + procaine 2% 1–2 ml + Mills' manipulation (20)	II Single injection of procaine 2% 1-3 ml + Mills' manipulation (20)	2 months	Assessor's global assessment on four-point ordinal scale: cured or improved	Positive	No significance testing performed; SR: (I) 70%, (II) 50%
Kivi (1982)[27]	32	occup-tional health center	I BM 1 ml + lidocaine 1 ml; maximum three injections (47) II Methylprednisolone 1 ml; maximum three injections (20)	II Indomethacin (NSAID) + wrist brace (+ 2 weeks) (21)	1 year	Patient's global assessment on four-point ordinal scale: good or excellent	Negative	No significant differences observed between I, II and III. SR: (I) 92%, (II) 85%, (III) 90%
Halle *et al* (1986)[25]	32	army clinic	I Single injection of HC + lidocaine (12)	II Ultrasound (12) III Ultrasound with iontophoresis (12) IV TENS (12)	5 days	Patient: percentage items improved on McGill pain questionnaire	Negative	There were no significant differences between I and II–IV. Also no significant differences on percentage improvement on McGill subscales. SR: (I) 63%, (II) 69%, (III) 65%, (IV) 56%.

*A higher VAS score means less favourable treatment result. OPD, outpatient department of hospital (referred patients); VAS, visual analogue scale; HC, hydrocortisone; BM, betamethasone; TC, triamcinolone; TENS, transcutaneous electrical nerve stimulation.

Table 4. Randomized clinical trials comparing different corticosteroid regimens for epicondylitis.

Reference	Review score	Setting	Corticosteroid injection A (number of patients available for follow-up)	Corticosteroid injection B (number of patients available for follow-up)	Follow-up duration	Determination of success rate	Authors' conclusion	Results
Price *et al* (1991a)[19]	63	OPD	I TC 10 mg + lignocaine 1 % 20 ml; 1 – 2 injections (27)	II TC 20 mg + lignocaine 1% 2 ml; 1 – 2 injections (30)	4, 8, 24 weeks	VAS pain 10 mm	Equal	Improvements in pain were similar, no significant differences. VAS pain* at 4 weeks: (I) 27 mm, (II) 29 mm, VAS pain* at 8 weeks: (I) 29 mm, (II) 22 mm; VAS pain* at 24 weeks: (I) 35 mm, (II) 33 mm
Hughes & Currey (1969)[28]	29	OPD	I Single injection of HC 1 ml = 25 mg + lignocaine 2% 1 ml (22)	II Hypospray HC 1 ml = 25 mg (28)	2 weeks	Global assessment by patient on three-point ordinal scale: success	Equal	No significant difference between I and II. SR: (I) 64%, (II) 64%. Injection less painful with hypospray: pain of injection: (I) 91%, (II) 58%

*A higher VAS score means less favourable treatment result. OPD, outpatient department of hospital (referred patients); VAS, visual analogue scale; HC, hydrocortisone; TC, triamcinolone.

corticosteroid injections are not unique.[16,17] The low scores on our checklist make it clear that there is much room for improvement in trials in this field, and the items on the checklist provide guidelines for improvement in future studies. Recent methodological research has shown that correct execution of the randomization procedure (item B) is of the utmost importance.[14] Similarity of important prognostic factors (item C), such as duration of the complaints and previous treatment,[2,34] is an important check on the adequacy of randomization and should be reported on in detail. A trial should be of sufficient size, as a small sample size (item F) reduces the power of a study to detect clinically relevant differences in effect between the interventions being tested. Moreover, small sample size might also lead to baseline incomparability of (unknown) prognostic factors, thereby causing biased results. Blinding of patients and physicians (item K) is of great importance in obtaining unbiased reporting of effects.[14] In the case of steroid injections, this seems difficult to establish. Most RCTs simply use a local anaesthetic as 'placebo'. However, as there is uncertainty about the possible specific effects of local anaesthetic in lateral epicondylitis, it should not be regarded as a proper placebo. A truly convincing placebo injection with similar opacity, (post-injection) pain sensation and viscosity would be the only guarantee of optimal blinding but seems to be difficult to create. Even if the patients and physicians cannot be blinded (insufficient placebo or a pragmatic comparison), appropriate assessment of the effects can be established by a blinded outcome assessor (item M). Given the natural history of lateral epicondylitis, with frequent recurrences and the relatively favourable course in the longer term, a trial should have a follow-up of at least 3 months (item N), but preferably 6 months or longer. The reviewed RCTs report positive short-term benefits (2–6 weeks), but after a longer follow-up, most of them fail to show the benefits of local steroid injections. This might mean that corticosteroid injections merely act as a painkiller with a long half-life, but do not provide definite cure. However, this finding may have a methodological background: most patients who have not fully recovered during the intervention period will probably receive one of the other trial treatments at a later date (e.g. placebo-treated patients will later be given corticosteroid injections) (contamination) or will start having treatment that was not included in the trial at all (co-intervention). Therefore, especially for the long-term follow up, adequate awareness of co-interventions and contamination (item J) is essential. In view of the methodological problems involved and the lack of positive results at follow-up exceeding 6 weeks, the long-term effectiveness of corticosteroid injections is not supported by scientific evidence.

Pooling

Although the general methodological quality of the trials was only moderate, we decided to pool the data of the RCTs. For the binary data needed for the pooling, we relied on different outcome measures. We adhered to a predetermined hierarchy in our choice of outcome measures, thereby limiting potential bias introduced in making such a choice. Although different outcome measures may measure different domains of a complaint, inspection of the data illustrates that the magnitude and direction of the outcomes finally used for the pooling closely resemble the main conclusions of the original authors of the trials involved. Therefore, we conclude that we did not introduce substantial bias in the selection of the outcome measures for pooling.

There are several ways of incorporating methodological quality in a meta-analysis.[13] Not to pool is an option.[16] However, recent trends in summarizing evidence support efforts to pool data.[35] We decided to perform a stratified analysis, with sub-sets of high and low methodological quality trials. This indicated an even greater effect for the trials of high methodological quality. Statistical testing revealed heterogeneity among the RCTs included in the (stratified) pooled analyses. Some plausible reasons for this heterogeneity are variation in study quality, differences in the type of patients included or the composition of the various injection fluids, variation in the number and interval of injections, different methods of outcome measurement and differences in the timing of the follow up. Given the status of current research in this field and the expectation that conclusive trials cannot be expected in the near future, we decided to pool the data in order to provide the reader with the most illustrative presentation of evidence currently available.

Study setting

Most studies were hospital based, with patients referred by general practitioners, which implies that filtering on the basis of prognostic patient characteristics (e.g. failure of treatment and chronicity of complaints) has most likely taken place. Although the direction and impact of this phenomenon is hard to assess, referral bias limits the possibility of generalizing the findings of this overview to the field of general practice.

Adverse effects

Local steroid injections are not an entirely innocuous type of treatment. The RCTs reported on two different side-effects: subcutaneous necrosis and post-injection pain. However, the reports were inconsistent with respect to subcutaneous necrosis. No findings were made by Verhaar,[2] whereas Price *et al*[19] found that 27% of patients suffered subcutaneous necrosis. However, there seems to be some over-reporting by the latter authors, as they also found subcutaneous necrosis in 17% of patients who received local anaesthetic injections. In conclusion, these figures do not allow quantification of the risk of this side-effect. Post-injection pain was a more frequently reported side-effect. The percentages reported for corticosteroid injections varied from 10%[22] (in combination with anaesthetic) to 50% for corticosteroids only.[19] Haker & Lundeberg[22] assume that post-injection pain is caused by both the volume effect of the injection and the corticosteroid itself. Using the same volume, Price *et al*[19] reported a much lower percentage of post-injection pain for local anaesthetic (11%) than for corticosteroid (50%), possibly indicating a specific irritation caused by injected corticosteroid. In the RCTs and also in daily practice the corticosteroid is injected either solely or in combination with a local anaesthetic, but unfortunately, no RCT directly compared these two options. Therefore, on the basis of studies included in our research, no advice can be given about the addition of an anaesthetic to the corticosteroid for the prevention of post-injection pain. On theoretical grounds, tendon rupture is an adverse effect that can occasionally be anticipated.[8,9] Our search strategy revealed no of this type in the international literature.

Composition

A variety of corticosteroid preparations were used in the RCTs. In the positive, methodologically higher ranking trials[2,19,22] triamcinolone was used. Price *et al*[19] found that 10 mg (compared with 20 mg) was sufficient. However, on empirical and theoretical grounds,[19] no clear difference in effectiveness compared with other long-acting preparations can be expected. The specific injection technique was generally too poorly described to give a clear recommendation based on the results of the trials. The same applies to the volume of the injection: the figures vary, generally between 1 and 2 ml was injected. No RCT included more than three injections. However, most RCTs included patients who had received corticosteroid injection before entry to the study. Three

injections seems to be the recommended maximum in several reviews,[7,8,9,36] although no studies have indicated an increase in adverse effects or a poor prognosis if more injections are given.

Conclusion

The existing evidence on corticosteroid injections for the treatment of lateral epicondylitis in primary care is not conclusive. Many trials are conducted in secondary care and have important methodological flaws. Corticosteroid injections appear to be relatively safe and seem to have a short-term effect (2–6 weeks) when used to treat patients referred to a hospital. The treatment seems to be suitable for application in general practice: it is easily administered and is relatively inexpensive. However, important questions regarding the optimal timing, dosage, injection technique and injection volume remain unanswered. Well-designed trials of sufficient size in general practice are needed to provide more evidence.

Appendix 1. Operationalization of the criteria.

A Study population defined by clearly described selection criteria (1 point). Restriction to a homogenous study population with respect to duration of complaint and previous treatments (3 points).

B Randomization procedure described (1 point). Randomization excludes bias (e.g. sealed envelopes, allocation by telephone, precoded packaged medication) (2 points).

C Study groups comparable for: duration of complaint (2 points), baseline scores for outcome measurements (2 points), age (1 point), previous treatment of complaint (2 points).

D Drop-outs: no drop-outs (3 points); number of drop-outs presented for each study group (1 point); reasons for withdrawal are given for each group (1 point).

E Percentage loss to follow-up:
100 – [(number of patients at main moment of effect measurement/number of patients at randomization) x 100]
Fewer than 20% in each group (1 point); fewer than 10% in each group (3 points).

F Size of the smallest study group after randomization (maximum 15 points).

G Description of: type of intervention (medication, type of physiotherapy, etc.) (4 points), schedule (4 points), duration of treatment sessions or number of injections (2 points).

H Comparison with a placebo intervention (5 points).

I Comparison between two or more regular, convincing interventions (5 points).

J Other (medical) interventions avoided in the design until moment of main effect measurement (5 points) or data on co-interventions presented and comparable between study groups (3 points).

K Blinding of patients and physician. Placebo injection indistinguishable: (pain) sensation or anaesthesia (1 point), volume (1 point), opacity (1 point). Convincing placebo injection separately or as component of a double dummy system. Blinding of patient evaluated and successful (1 point), blinding of physician evaluated and successful (1 point).

L Outcome measures presented: pain (2 points), global measure of improvement (2 points), functional status (2 points), grip strength (2 points), adverse reactions (2 points).

M Outcome assessor adequately blinded for treatment allocation (5 points). Blinded assessment of each outcome measure mentioned under L (1 point each).

N Timing of effect measurement identical for all study groups (3 points). Final effect measurement at least 3 months after randomization (2 points).

O Intention-to-treat analysis. When loss to follow-up $\leq$ 10%: analysis of results on all randomized patients for most outcome measures, and on the most important moments of effect measurement, irrespective of drop-outs or missing values. When loss to follow-up > 10%: intention-to-treat analysis plus alternative analysis, e.g. worst case analysis, which accounts for drop-outs and missing values (5 points).

P Frequencies, or mean and standard error of the mean or standard deviation, or median and quartiles of most important outcome measures presented for each treatment group at most important moments of effect measurement (5 points).

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