Local corticosteroid injection for carpal tunnel syndrome (Review)

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ABSTRACT

Background
Carpal tunnel syndrome is a clinical syndrome manifested by signs and symptoms of irritation of the median nerve at the carpal tunnel in the wrist. Local corticosteroid injection for carpal tunnel syndrome has been studied but its effectiveness is unknown.

Objectives
To evaluate the effectiveness of local corticosteroid injection for carpal tunnel syndrome versus placebo injection or other non-surgical interventions.

Search strategy
We searched the Cochrane Neuromuscular Disease Group Trials register (searched May 2006), MEDLINE (searched January 1966 to May 2006), EMBASE (searched January 1980 to May 2006) and CINAHL (searched January 1982 to May 2006).

Selection criteria
Randomized or quasi-randomized studies.

Data collection and analysis
Three authors independently selected the trials and rated their overall quality. Relative risks and 95% confidence intervals were calculated for each trial and summary relative risks and 95% confidence intervals were also calculated.

Main results
We included 12 studies with altogether 671 participants. Two high quality randomized controlled trials with altogether 141 participants demonstrated clinical improvement of carpal tunnel syndrome at one month or less following local corticosteroid compared to placebo injection (relative risk 2.58 (95% confidence intervals 1.72 to 3.87)). One trial compared local corticosteroid injection to oral corticosteroid and at 12 weeks after treatment there was significantly more improvement in the injection group (mean difference -7.10 (95% confidence intervals -11.68 to -2.52)). In one trial, the rate of improvement after one month was greater after local than systemic corticosteroid injection (relative risk 3.17 (95% confidence intervals 1.02 to 9.87)). In one trial, symptoms did not improve significantly more in the injection group at eight weeks after injection compared to treatment with anti-inflammatory medication and splinting (mean difference 0.10 (95% confidence intervals -0.33 to 0.53)). Two injections versus one injection of local corticosteroid did not provide further clinical improvement, mean difference -3.80 (95% CI -9.27 to 1.67).

Authors' conclusions
Local corticosteroid injection for carpal tunnel syndrome provides greater clinical improvement in symptoms one month after injection compared to placebo. Significant symptom relief beyond one month has not been demonstrated. Local corticosteroid injection provides significantly greater clinical improvement than oral corticosteroid for up to three months. Local corticosteroid injection does not significantly improve clinical outcome compared to either anti-inflammatory treatment and splinting after eight weeks or Helium-Neon laser treatment after six months. Two local corticosteroid injections do not provide significant added clinical benefit compared to one injection.

PLAIN LANGUAGE SUMMARY

Local corticosteroid injection is effective in the short-term for the treatment of carpal tunnel syndrome

Local corticosteroid injection is a common non-surgical treatment for carpal tunnel syndrome. Other non-surgical treatments include the use of wrist splints, ultrasound and oral anti-inflammatory agents. Surgical intervention is also known to be effective. This systematic review confirmed the effectiveness of local corticosteroid injection for relief of symptoms for severe carpal tunnel syndrome up to one month after injection. Local corticosteroid injection provides significantly greater clinical improvement compared to oral corticosteroid up to three months after treatment. Two injections of local corticosteroid do not provide significant further clinical improvement of symptoms. Further research is required to determine length of benefit of local corticosteroid injection and benefit for mild and moderate carpal tunnel syndrome.

BACKGROUND

Carpal tunnel syndrome (CTS) is a clinical syndrome manifested by signs and symptoms of irritation of the median nerve at the level of the carpal tunnel in the wrist. These include paraesthesiae, pain and numbness in the fingers and thumb in the distribution of the median nerve (Rosenbaum 1993). The severity of CTS ranges from mild to severe. Mild carpal tunnel syndrome presents as intermittent symptoms whereas severe CTS can cause permanent loss of sensation and partial paralysis of the thumb. Carpal tunnel syndrome is a very common problem encountered in industrialized populations. A Swedish study determined the prevalence of clinically certain CTS in the general population to be 3.8% (95% CI 3.1 to 6.4%) (Atroshi 1999). Two recent studies have confirmed high incidence rates in the general population where Bland and Rudolfer demonstrated a rate of 61.5 to 120.5/100,000 women and 35 to 60 cases per 100,000 men in the United Kingdom (Bland 2003). Mondelli et al. (Mondelli 2002) identified an even higher incidence rate in the Italian general population of 139 cases per 100,000 men and 506 cases annually per 100,000 women. Bland and Rudolpher (Bland 2003) also noted increasing incidence rates but suggested that this was likely to be related to the identification of more mild cases of CTS.

The natural history of CTS has not been well studied. In one study, up to one third of participants had spontaneous improvement of their symptoms without any formal medical treatment (Futami 1992). More recently, Padua et al. have confirmed that a number of persons with CTS improve spontaneously without treatment and a short duration of symptoms is a positive prognostic indicator (Padua 2001). In this prospective study, for those participants who did not have surgical treatment, 34% had symptom improvement and 45% of participants had stationary symptoms over one year. The treatment of CTS falls into two broad categories, surgical or non-surgical. Surgical treatment is generally preferred in severe cases of CTS, whilst non-surgical treatment is usually initiated for mild to moderate CTS (Duncan 1987). Examples of non-surgical treatments include wrist splints, oral non-steroidal anti-inflammatory agents and local corticosteroid injection into the carpal tunnel.

Corticosteroid injection into the carpal tunnel has been studied but most studies are either retrospective in design or prospective but non-randomized (Giannini 1991; Kaplan 1990; Van Rossum 1980; Weiss 1994). The effectiveness of corticosteroid injection is not known and recurrence rates of symptoms have varied from eight to 100% (Girlanda 1993). This variation in the effectiveness of local corticosteroid injection could be due to a number of reasons such as outcome measures, trial design and patient population examined. Since the prevalence of mild to moderate CTS is high, the impact of this conservative intervention could be significant for managing the syndrome. Also since a significant proportion of CTS cases resolve spontaneously, only controlled trials will provide evidence for the true effectiveness of this intervention.

This systematic review will evaluate the effectiveness of local corticosteroid injection of the carpal tunnel for relieving symptoms and preventing eventual surgical treatment.

OBJECTIVES

Primary

To evaluate the effectiveness of local corticosteroid injection for CTS versus placebo injection or other non-surgical interventions in improving clinical outcome.

Secondary

To determine the length of symptom relief following corticosteroid injection into the carpal tunnel.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

We included only randomized, or quasi-randomized, controlled trials.

Types of participants

Participants must have had CTS diagnosed in one or both hands and will not have had previous flexor retinaculum release. Partici-

pants will not have had other peripheral nervous system disorders such as polyneuropathy. Only studies evaluating treatment for idiopathic CTS were included.

Diagnosis of carpal tunnel syndrome used by authors was accepted but the preferred criteria conformed to the 'Practice parameter for carpal tunnel syndrome' published by the Quality Standards subcommittee of the American Academy of Neurology (AAN 1993).

Diagnostic Criteria

History

A. Symptoms

1. Dull aching discomfort in the hand, forearm or upper arm
2. Paraesthesiae in the hand
3. Weakness or clumsiness of the hand
4. Dry skin, swelling, or colour changes in the hand
5. Occurrence of any of these symptoms in the distribution of the median nerve

B. Provocative factors

1. Sleep
2. Sustained arm or hand positions
3. Repetitive actions of the hand or wrist

C. Mitigating factors

1. Changes in hand posture
2. Shaking the hand

Physical examination

A. May be normal

B. Symptoms elicited by tapping or direct pressure over the median nerve at the wrist (Tinel's sign) or with forced flexion or extension of the wrist (Phalen's sign)

C. Sensory loss in the median nerve distribution

D. Weakness or atrophy in the thenar muscles

E. Dry skin on the thumb, index or middle fingers

Confirmatory tests

A. Electromyography and nerve conduction studies (NCS) which can confirm a median neuropathy at the wrist but are not able to exclude the diagnosis of carpal tunnel syndrome.

Types of intervention

The treatment intervention was local corticosteroid injection into or near the carpal tunnel.

Types of outcome measures

The primary outcome measure was clinical improvement at three months follow-up, preferably demonstrated through functional or quality of life measures.

Secondary outcome measures included:

(1) Improvement in neurophysiologic parameters

(2) Clinical improvement at less than three months follow-up

(3) Clinical improvement at one year follow-up

(4) Requirement of surgery for flexor retinaculum release

(5) Improved quality of life

(6) Delay until return to employment

In future updates of this review, adverse events will be specifically identified as an outcome.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: Cochrane Neuromuscular Disease Group methods used in reviews.

We searched the Cochrane Neuromuscular Disease Group Trials Register for randomized controlled trials using 'carpal tunnel syndrome' as the search term (May 2006).

A computer search (May 2006) was conducted using MEDLINE (January 1966 to May 2006), EMBASE (from January 1980 to May 2006) and CINAHL (January 1982 to May 2006). For electronic search strategies, see Table 01.

The bibliographies of all papers identified by these strategies were searched. Where possible authors of identified papers were contacted to determine if other relevant studies may be available. A search for unpublished articles was made by contacting the Canadian Society of Clinical Neurophysiology and the American Association of Electrodiagnostic Medicine.

METHODS OF THE REVIEW

Three authors (SM, GT, NA) independently selected the trials to be included in the study. Attempts were not made to blind the review authors with regard to trial authors, institution or journal. Disagreements were resolved by discussion followed by consensus of the review authors.

To assess methodological quality, the 'Quality Assessment of RCTs' scale developed by Jadad (Jadad 1994) was used by the authors (SM, GT, NA) and a consensus reached for the quality score.

Data collection

Data were independently collated by the authors using data extraction sheets and entered into a computerized database. Data were cross checked by all authors.

Data synthesis

Review Manager (RevMan) software was used for the statistical analysis. Studies were compared for heterogeneity using the Chi-square statistic. Sensitivity analyses were performed based on the methodological quality score and individual factors such as allocation concealment. Relative risks were calculated for dichotomous outcomes and weighted mean differences for continuous outcomes. Studies were assessed for heterogeneity using the Chi square statistic. If genuine heterogeneity not due to clear differences between the types of subjects, methods of intervention or study design were found, random effects analyses

were used. Otherwise the analyses were performed assuming a fixed effect. Subgroup analyses would have been performed but the information available did not allow this analysis. The results of comparable trials were pooled to provide a point estimate.

DESCRIPTION OF STUDIES

A total of 25 controlled trials have been identified as having potential for inclusion in this review. All trials were identified from the published literature. Twelve studies have been included in this review, 10 have been excluded and three are currently awaiting assessment.

Excluded Studies

Ten potential studies have been excluded from this review. Two of these studies were excluded (Hui 2005; Ly-Pen 2005) since the focus was on corticosteroid injection versus surgery and were more appropriate for the Cochrane review (Verdugo 2003) comparing surgical and non-surgical interventions for the treatment of carpal tunnel syndrome. One of the excluded trials (Wu 1991) used only electrophysiologic measures as the primary outcome measure and did not record change in clinical symptoms as an outcome measure. The study by Girlanda et al. (Girlanda 1993) did record change in clinical symptoms but did not report individual patient outcomes, but only significance levels for comparing the intervention and control groups to their baseline clinical symptoms. Attempts to contact the authors in order to obtain the original data were unsuccessful. The study by Elbaz et al. (Elbaz 1994) was excluded since only a published abstract with limited data could be identified. Attempts to contact the authors for further information were unsuccessful. A study of local corticosteroid injection by Piotrowski et al. (Piotrowski 1998) was excluded since this study primarily focussed on the adverse effects of local injection and only included a minority (25 of 158 injections) of CTS cases. Three more recently identified studies were not included in this review, since they did not have control groups (Agarwal 2005; Graham 2003; Hagebeuk 2004). The study Dammers 2001 is only available as an abstract.

Included Studies

The setting for one of the included studies, comparing corticosteroid injection to placebo injection (Dammers 1999) was an outpatient neurology clinic in the Netherlands where 84% of the participants were female. Although Dammers (Dammers 1999) used peripheral nerve conduction studies to confirm CTS, specific criteria for diagnosis of CTS were not identified. Participants had to have had symptoms for at least three months duration. Severity of CTS was not addressed, but absence of sensory nerve action potentials on electrodiagnostic testing for 80% of participants suggested severe CTS. This study used short acting injectable corticosteroid. Dammers et al. injected 40 mg of methylprednisolone with 10 mg of lignocaine or 10 mg of lignocaine 4 cm proximal to the wrist crease. The primary outcome was clinical assessment, estimated by subjective report of clinical severity. The clinical outcome was the answer to the question whether their symptoms were absent or only minor not requiring treatment or significant enough to require further treatment. Outcomes were recorded at one month with further outcomes measured up to one year.

Similar to Dammers 1999, Armstrong et al. (Armstrong 2004) performed a double-blinded placebo-controlled trial comparing corticosteroid to placebo injections. Only those participants with symptoms of CTS and abnormal NCS were offered entry into the trial. At study commencement, participants completed the Carpal Tunnel Study Functional Status and Symptom Severity Questionnaire. Participants were randomly assigned to the betamethasone (1 ml containing 6 mg) or the placebo group (1 ml saline). Outcomes were initially measured at two weeks with a tolerance of four days. Patient satisfaction with the degree of symptom relief was the primary outcome measured using a five-point scale. Secondary outcomes included (a) changes in NCS and (b) changes in scores on the Carpal Tunnel Study Functional Status and Symptom Severity Questionnaire. Results of initial outcome measures dictated the next treatment phase of the trial. Participants who had received corticosteroid injection and were not satisfied with symptom relief were referred for surgical intervention. Participants who received corticosteroid injections and were highly or somewhat satisfied were enrolled in an 18 month longitudinal study of repeat corticosteroid injections. Placebo participants who were not satisfied with symptom relief were offered corticosteroid injection. Of these participants, those that responded positively to corticosteroid injection were further enrolled in the 18 month longitudinal study. The remainder were referred to surgery. Those participants who initially received placebo and were satisfied with symptom relief were offered either corticosteroid injection or referral to surgery for recurrent symptoms.

One study compared local corticosteroid injection to a single systemic corticosteroid injection (Ozdogan 1984) in a rheumatology out-patient clinic in Turkey. All the participants were female. Ozdogan (Ozdogan 1984) used the symptoms of burning and tingling in the thumb, index and long (sic) fingers in conjunction with nocturnal symptoms to confirm the diagnosis. Peripheral NCS were not used. Betamethasone disodium phosphate and acetate suspension (1.5 mg) or an equal volume of saline was injected into the carpal tunnel just proximal to the palm. In this study participants were also injected in the ipsilateral deltoid muscle with the active medication for those who had placebo injected into the carpal tunnel and saline was injected for those who had received betamethasone. Dosages and volumes injected into the deltoid were the same as for those directed to the carpal tunnel. The primary outcome was clinical assessment, estimated by subjective report of clinical severity. Ozdogan (Ozdogan 1984) used an ordinal ranking scale of symptoms including the terms nil, minimal, moderate and severe. Outcomes were determined at one month after injection.

Wong et al. (Wong 2001) completed a double blinded, randomized controlled trial comparing local corticosteroid injection and oral corticosteroid. The local injection consisted of 15 mg of methylprednisolone injected into the carpal tunnel whereas the oral group received prednisolone 25 mg daily for 10 days. The primary outcome used was the Global Symptom Score at two, eight and 12 weeks. This outcome measure was based on rating the severity of five symptoms (pain, numbness, paresthesia, weakness/clumsiness and nocturnal awakening) on a scale from 0 to 10. These scores were added to provide a total score ranging from 0 (absence of symptoms) to 50 (most severe symptoms).

Celiker et al. (Celiker 2002) completed an unblinded, randomized controlled trial comparing local corticosteroid injection with the anti-inflammatory medication, acemetacine and splinting. Participants in the injection group received local injection, 4 cm proximal to the wrist crease, of 40 mg of methylprednisolone. In the comparison group, participants received acemetacine 120 mg/day and also were provided with a light weight, neutral angle wrist splint to be worn at night. The main outcome measure used was the Symptom Severity Scale and secondary outcome measures included NCS, Visual Analog Scale for pain, Tinel's sign and Phalen's test. A Symptom Severity Scale measured symptoms based on eleven questions each rated from one to five. The overall score was the mean of the scores for each question. Outcomes were recorded at two and eight weeks after the start of the trial.

Lucantoni et al. (Lucantoni 1992) used an unblinded, randomized controlled trial to compare local corticosteroid injection to Helium-Neon Laser treatment. In the local injection group participants were injected with methylprednisolone 20 mg at the level of the carpal tunnel at baseline and the injection was repeated at 10 days. The laser group received daily 20 minute Helium-Neon Laser treatments at a frequency of 3000 Hz. The treatments lasted for 20 days. The primary outcome was symptom improvement and secondary outcomes were based on NCS recorded at 20 days and six months after the start of the trial.

O'Gradaigh and Merry (O'Gradaigh 2000) performed a randomized controlled single blind trial of low versus high dose and short versus long acting corticosteroids. Included participants had abnormal CTS or positive Phalen or Tinel tests combined with classic distribution of symptoms. Participants received a 1 ml injection without lignocaine using a 23G needle inserted at the distal carpal skin crease immediately ulnar to the palmaris longus tendon. In the first phase of the trial, participants in Group A received 25 mg of hydrocortisone, Group B received 100 mg of hydrocortisone and Group C had no injection. In Phase two, participants in Group D received 20 mg of triamcinolone, and Group E received 100 mg of hydrocortisone. Participants were assessed at six weeks and six months. The primary outcome was a subjective change in symptoms measured using a five-point scale. Secondary outcomes included changes in NCS and a change from a positive to a negative Phalen or Tinel test.

Habib et al. (Habib 2006) completed a randomized, unblinded trial of two different injection techniques. The injection technique varied in two ways. Group 1 (n = 21) was injected with a higher dose of methylprednisolone acetate (35 mg) and lidocaine 2% (0.5 ml) at the wrist crease. Group 2 (n = 21) was injected with only 15 mg of methylprednisolone acetate and 0.15 ml of lidocaine 2% at a location two to three cm distal to the wrist crease. Outcomes included symptomatic improvement at 1, 3, 6 and 12 weeks as well as rating of pain from the injection.

Wong et al. (Wong 2005) completed a double blinded randomized controlled trial comparing the effect of single versus two consecutive local corticosteroid injections. All participants were initially randomized to the single or double injection group and were advised that they would receive two injections (active/ active or active/placebo). The single injection group was not advised of the order in which they would receive the active medication for injection. All participants were first injected with 15 mg of methylprednisolone and then after eight weeks the double injection group had the same injection repeated whereas the placebo group had a similar volume of saline injected under double blind conditions. The primary outcome for the study was Global Symptom Score which was recorded at eight, 24 and 40 weeks after the second injection.

Sevim et al. (Sevim 2004) carried out a single blinded study that attempted to compare the effectiveness of nocturnal splinting versus local corticosteroid injection. Participants with the clinical diagnosis of CTS confirmed with electrodiagnostic studies were randomized at baseline to one of three groups. The splint group (n = 60) were instructed to wear a neutral angle wrist splint at night for the duration of the study. The distal injection group (n = 30) were injected at the anterior wrist flexion crease with 3 mg betamethasone disodium phosphate and 3 mg betamethasone acetate suspension mixed with 0.5 cc of lidocaine HCL 2% solution. The proximal injection group was injected with the same medication on the volar surface of the forearm 4 cm proximal to the wrist crease. Outcome measures for this study included NCS as well as the Neurologic Symptom Score which were assessed at approximately 11 months after treatment. The investigators for this study created a control group from participants in the splinting group who did not comply with wearing of splints and dropped results for those who partially complied. This departure from intent to treat effectively neutralized any benefits of randomization initially done for the splinting group and therefore data from the splinting groups could not be used for this review.

Gökoglu et al. (Gokoglu 2005) evaluated the effect of iontophoresis with topical corticosteroid compared to local corticosteroid injection. This unblinded randomized controlled trial included 30 participants with the clinical diagnosis of CTS confirmed by electrodiagnostic studies. The injection group received an injection of 40 mg of methylprednisolone acetate at the level of the carpal tunnel. A solution of 0.4% dexamethasone phosphate was applied

over the carpal tunnel for the iontophoresis group and treatment was maintained at an amplitude of 40 to 45 mA for 20 minutes, every other day for one week. Outcomes were assessed at two and eight weeks following the start of the trial. The outcome measures included the Symptom Severity Score, the Functional Status Scale and a pain Visual Analog Scale.

Aygül et al. (Aygul 2005) completed an unblinded randomized controlled trial comparing local corticosteroid injection, iontophoresis and phonophoresis. Thirty-three women with the clinical diagnosis of CTS confirmed with electrodiagnostic studies were enrolled. Treatment intervention groups were local corticosteroid injection, iontophoresis or phonophoresis. Treatments lasted 10 minutes and were applied five days per week for three weeks. Local corticosteroid injection (n = 12) into the carpal tunnel involved 1 mL dexamethasone sodium phosphate without local anaesthetic. Iontophoresis (n = 10) was carried out as a single therapy with 1 to 4 mA galvanic current applied over the carpal tunnel with a pad soaked in 0.1% dexamethasone sodium phosphate covering the positive electrode. The therapy sessions lasted 10 minutes and were administered five days a week for three weeks. The phonophoresis group (n = 11) similarly received treatment at 3 MHz and intensity of 1.0 W/cm^2 and 0.1% dexamethasone sodium phosphate. Treatment outcomes included the Symptom Severity Score and the Functional Status Score. Electrophysiological outcomes were also reported, but, the investigators reported these as dichotomous outcomes (significant improvement) rather than mean values and standard deviations.

Summaries of the trials are given in the 'Table of included studies'.

Studies Awaiting Assessment

Three randomized controlled trials, have been placed in this category and await assessment (Hui 2004; Nalamachu 2006; Tuncay 2005). Two of these studies meet the inclusion criteria for this review, but the published data are provided only in a graphic format which cannot be used for this review (Hui 2004; Nalamachu 2006). The authors have been contacted for original data. The study by Tuncay (Tuncay 2005) is only available in abstract and will be obtained.

METHODOLOGICAL QUALITY

Overall, there is quite a variation in the quality of studies included in this review. A number of studies could be considered to be of good quality (Please see Table 02). The Ozdogan (Ozdogan 1984) trial was scored at four out of five with the quality assessment form developed by Jadad (Jadad 1994) since, the method of randomization and concealment of treatment allocation were not adequately described. Wong 2001 comparing oral versus local injection of corticosteroid yielded a high quality rating of five out of five. The Wong 2005 study scored four out of five with one point lost for not identifying the method of randomization. The initial phases of the Dammers 1999 and Armstrong 2004 studies scored five out of five points. However in Dammers 1999 93% of the placebo injection group had been unblinded for the study by three months after injection. Similarly in Armstrong 2004 participants were unblinded after the initial treatment phase. For each of these studies, subjective clinical symptom improvement was the primary outcome. Baseline characteristics such as mean age and duration of symptoms for the control and active treatment groups were similar for each study. The spectrum of severity of CTS was alluded to in the Dammers study by the reporting of absence or presence of median sensory nerve action potentials on electrodiagnostic studies.

Blinding tended not to be undertaken in trials comparing alternative active treatment interventions with local corticosteroid injection therefore tending to lead to poor overall quality ratings. In Celiker 2002 the inability to blind resulted in a quality score of three out of five. The Aygul 2005 (two out of five), Sevim 2004 (one out of five), Gokoglu 2005 (one out of five), O'Gradaigh 2000 (one out of five), Habib 2006 (two out of five) and Lucantoni 1992 (one out of five) studies were of even lower quality. They did not use blinding, did not describe randomization procedures, or account for withdrawals (with the exception of Aygul 2005).

RESULTS

Ten of the 12 included RCTs evaluated outcomes at less than three months following treatment, whereas only eight of the eleven studies provided outcomes at three months or greater after treatment.

Symptom improvement one month or less after injection compared to placebo

In one study comparing local corticosteroid injection to placebo injection, the symptom severity one month after injection was the primary outcome measure (Dammers 1999) (n = 60 participants). One month following injection there was significant improvement in the local corticosteroid injection versus placebo injection group with a relative risk (RR) of 3.83 (95% CI 1.82 to 8.05). In a second study, Armstrong 2004 (n = 81 participants) there was significant clinical improvement at two weeks following local injection with 1 mL of betamethasone compared to placebo injection, RR 2.04 (95% CI 1.26 to 3.31). Taken together, these studies show significantly more participants with improvement after corticosteroid injection than placebo, RR 2.58 (95% confidence intervals 1.72 to 3.87) (Analysis 01.01).

Local corticosteroid injection compared to systemic corticosteroid

Daily oral corticosteroids versus local injection were compared by Wong 2001 (n = 60 participants). Comparison at two weeks did not demonstrate a significant difference in Global Symptom Score between local injection and oral corticosteroid. The mean difference (MD) was -4.20 (95% CI -8.66 to 0.26) (Analysis 02.01.01). However, at eight weeks and 12 weeks after treatment onset, local

corticosteroid treatment was found to be significantly better than oral corticosteroid, mean difference -7.16 (95% CI -11.46 to -2.86) (Analysis 02.01.02) and -7.10 (95% CI -11.68 to -2.52) (Analysis 02.01.03) respectively.

Ozdogan 1984 (n = 37 participants) compared local corticosteroid injection versus single systemic corticosteroid injection. The primary outcome measure was symptom severity rated on an ordinal scale. At one month following injection, there was significant improvement in symptoms for the group undergoing local versus systemic injection, RR 3.17 (95% CI 1.02 to 9.87) (Analysis 02.02).

Local corticosteroid injection compared to oral anti-inflammatory and neutral angle wrist splint

Celiker 2002 compared local corticosteroid injection with oral anti-inflammatory drugs and neutral angle wrist splint. Clinical severity was rated using the Symptom Severity check list score as the primary outcome measure. For this study, some participants received intervention in each hand, resulting in 23 participants and '37 hands' in the study. No significant difference was found in clinical outcome two weeks, MD 0.00 (95% CI -0.64 to 0.64) (Analysis 03.01.01), or eight weeks, MD 0.10 (95% CI -0.33 to 0.53) (Analysis 03.01.02) after start of treatment. Secondary outcome measures including the Visual Analog Score for Pain, NCS values and physical findings including Tinel's sign and Phalen's test did not differ significantly (Analyses 03.02 to 03.06).

Local corticosteroid injection compared to Helium-Neon laser treatment

In Lucantoni 1992 (n = 40), local corticosteroid provided significantly greater clinical improvement than He-Ne laser RR 1.89 (95% CI 1.12 to 3.17) (Analysis 04.01) at two weeks after onset of treatment. However, there was no significant difference in clinical outcome after six months, MD 0.75 (95% CI -2.81 to 4.31) (Analysis 04.02). Similarly at six months follow up there was no significant difference between groups for NCS values.

Low dose corticosteroid injection compared to high dose corticosteroid injection

At six weeks after injection there was no difference in subjective clinical improvement between high dose versus low dose injection, combined RR 1.00 (95% CI 0.76 to 1.31) (Analysis 05.01.03) (Habib 2006 (n = 42); O'Gradaigh 2000 (n = 64)). O'Gradaigh (O'Gradaigh 2000) compared low dose (25 mg hydrocortisone) injection into the carpal tunnel versus high dose (100 mg hydrocortisone) measuring outcome at six weeks after injection. Clinical symptoms were not significantly different for either treatment group, RR 1.05 (95% CI 0.73 to 1.52) (Analysis 05.01.03). Although follow-up at six months was reported, the investigators only evaluated those who had responded at six weeks, therefore, these data were not used. Another study examined the effect of 15 mg versus 35 mg of methylprednisolone injected into the carpal tunnel, but a confounding factor was that both the dosage and site (proximal (higher dose) to the wrist crease versus distal (lower dose) to the wrist crease) were different (Habib 2006). No difference in subjective clinical outcome was noted at 1 week (RR not estimable), 3 weeks, RR 0.88 (95% CI (0.63 to 1.24), 6 weeks, RR 0.93 (95% CI 0.62 to 1.40), or 12 weeks, RR 1.00 (95% CI 0.59 to 1.69) (Analysis 05.01.01 to 05.01.04).

Short-acting corticosteroid injection compared to long-acting corticosteroid injection

One study compared long acting local corticosteroid (20 mg triamcinolone) versus short acting local corticosteroid (100 mg hydrocortisone) injection into the carpal tunnel and measured outcome after six weeks after injection (O'Gradaigh 2000) (n = 39). Clinical symptoms were not significantly different for either treatment group, RR 1.08 (95% CI 0.71 to 1.64) (Analysis 06.01). Although follow-up at six months was reported, the investigators only evaluated persons who had responded to treatment at six weeks so that these data were not used.

Single versus two local corticosteroid injections

Wong et al. (Wong 2005) (n = 40) did not demonstrate a significant difference in patient outcome in the Global Symptom Score between groups receiving repeat local injection of 15 mg of methylprednisolone acetate versus placebo injection with follow up occurring at eight weeks, MD -3.80 (95% CI -9.27 to 1.67) (Analysis 10.01.01), 24 weeks, MD -2.90 (95% CI -9.20 to 3.40) (Analysis 10.01.02) and 40 weeks, MD 1.50 (95% CI -4.76 to 7.76) (Analysis 10.01.03) after injection.

Proximal versus distal local corticosteroid injection into the carpal tunnel

One study compared injection four centimetres proximal to the wrist flexor crease and distal injection at the anterior wrist flexion crease (Sevim 2004) (n = 57). At 11 months after injection, there was no significant difference between groups based on the clinical Neurologic Symptom Score, WMD 2.17 (95% CI -1.07 to 5.41) (Analysis 11.01). There was also no significant differences in electrophysiological outcomes at the same time (Analyses 11.02 to 11.04). Habib et al. (Habib 2006) compared two techniques of injection with the confounding factor that both site and dosage varied between randomized groups. There was no significant difference in subjective clinical symptom outcome between injection proximal or distal to the wrist crease at 1week (RR not estimable), 3 weeks, RR 0.88 (95% CI (0.63 to 1.24) (Analysis 08.01.02), 6 weeks, RR 0.93 (95% CI 0.62 to 1.40) (Analysis 08.01.03), or 12 weeks, RR 1.00 (95% CI 0.59 to 1.69) (Analysis 08.01.04).

Local corticosteroid injection versus iontophoresis

Two low quality studies (Jadad quality scores 2 or less) have compared local corticosteroid injection to iontophoresis for treatment of CTS (Aygul 2005 (n = 21)) (Gokoglu 2005 (n = 30)). At two weeks after injection, the study by Gokoglu demonstrated a significant improvement in the Symptom Severity Score, WMD -0.60 (95% CI -1.18 to -0.02) (Analysis 07.01.01), but there was no difference in the Functional Status Score, WMD -0.60 (95% CI-1.24 to 0.04) (Analysis 07.02.01) or Visual Analog Scale score

for pain, WMD -0.60 (95% CI -1.23 to 0.03) (Analysis 07.03.01) (Gokoglu 2005). At eight weeks after treatment, two studies show no difference in outcome between injection and iontophoresis for the Symptom Severity Scale, WMD -0.29 (95% CI -0.63 to 0.05) (Analysis 07.01.02) and the Functional Status Score, WMD -0.28 (95% CI -0.95 to 0.39) (Analysis 07.02.02). However, the pain Visual Analog Scale demonstrates significant benefit in the injection group compared to the iontophoresis group at eight weeks, WMD -1.70 (95% CI -2.38 to -1.02) (Analysis 07.03.02). Aygul et al. (Aygul 2005) compared electrodiagnostic study results between groups at two months, RR 2.93 (95% CI 1.16 to 7.36) (Analysis 07.13.01) and four months, RR 2.52 (95% CI 1.13 to 5.60) (Analysis 07.13.02). After treatment the results showed a significant improvement in sensory conduction latency difference between digits 2 (median nerve) and 5 (ulnar nerve) at each of these times, however multiple other tests were not significant.

Local corticosteroid injection versus phonophoresis

Aygul et al. (Aygul 2005) (N = 22) compared local corticosteroid injection and phonophoresis and did not demonstrate any significant differences after two months or four months between treatment groups based on the Symptom Severity Score, WMD at two months -0.30 (95% CI -0.78 to 0.18) (Analysis 09.01.01) and at four months WMD -0.40 (95% CI -0.93 to 0.13) (Analysis 09.01.02) and Functional Status Score, WMD at two months 0.00 (95% CI -0.31 to 0.31) (Analysis 09.02.01) and four months, WMD -0.17 (95% CI -0.53 to 0.19) (Analysis 09.02.02). Once again multiple comparisons between groups for electrodiagnostic studies were made. At four months after treatment, a significant difference favouring injection was found for the median/ ulnar nerve sensory amplitude ratio, RR 2.70 (95% CI 1.06 to 6.88) and the sensory latency difference between digits 2 and 5, RR 2.52 (95% CI 1.13 to 5.60) (see Table 03).

DISCUSSION

Comparison with placebo

This review includes two good quality randomized controlled trials (Armstrong 2004; Dammers 1999) that demonstrate significant symptom relief for CTS as a result of local corticosteroid injection after two weeks to four weeks, RR 2.58 (95% CI 1.72 to 3.87) compared to placebo injection. There were no adverse events reported in these trials.

The duration of symptom relief for CTS following local corticosteroid injection cannot be reliably commented upon beyond one month post injection. Although the study by Dammers (Dammers 1999) followed up patients to one year after injection, comparisons between the active and placebo groups were not possible beyond one month. At that time blinding was broken for treatment non-responders and corticosteroid injection was offered to those who had received placebo. In the open portion of the study, 50% of participants in the intervention group, one year after injection, had not required further treatment. Non-responders in the control group were given local corticosteroid injection and 24 of 28 participants had relief of symptoms. One year after injection, 12 (50%) of these subjects had not required further treatment for their CTS symptoms. A similar scenario occurred in the Armstrong study (Armstrong 2004): some participants were followed up to 18 months and had repeat corticosteroid injections for recurrent symptoms. Participants who initially received placebo were offered corticosteroid injection or referral to surgery for recurrent symptoms. These results are similar to other non-controlled trials which have shown symptom relief beyond one month (Agarwal 2005; Ayhan-Ardic 1996; Babu 1994; Gelberman 1980; Giannini 1991; Green 1984; Irwin 1996; Manz 1974; Matulova 1989; Mortier 1989; Seror 1992; Weiss 1994). Hayward (Hayward 2000) criticised the study by Dammers (Dammers 1999) because it did not demonstrate that corticosteroid injection is more effective than placebo after three months. Previous trials have shown improvement after a number of months of non-surgical treatment (Destefano 1997). Although not included in the analysis, the studies by Wu (Wu 1991) and (Girlanda 1993) further support the effectiveness of local corticosteroid injection for treatment of CTS. Wu (Wu 1991) demonstrated electrophysiological improvement compared to controls following injection, but did not evaluate symptom improvement. Girlanda (Girlanda 1993) also demonstrated significant clinical improvement at one and two months after local corticosteroid injection compared to controls.

Comparison with other interventions

The study by Wong et al. (Wong 2001) supports the effectiveness of local corticosteroid treatment for CTS and actually demonstrates benefit compared to oral corticosteroid up to 12 weeks after injection. In the short term, oral corticosteroids have been demonstrated to be effective in managing CTS symptoms (Chang 1998; Herskovitz 1995; Hui 2001), but it appears that the duration of effect for local corticosteroid injection is superior. However, benefit beyond the three month time frame remains unknown.

As identified above, the study by Dammers et al. (Dammers 1999) suggests a possible long term benefit, but this is in contrast to other results such as those found by Lucantoni (Lucantoni 1992) where benefit of corticosteroid injection compared to Helium-Neon laser is not maintained at 6 months follow-up.

In a unique study comparing local corticosteroid injection and single systemic/ intramuscular corticosteroid injection, benefit is demonstrated up to one month after injection for local corticosteroid injection (Ozdogan 1984).

Comparison of local corticosteroid injection to anti-inflammatory and neutral angle wrist splints confirms clinical improvement from baseline, but does not demonstrate that one treatment is superior to the other (Celiker 2002). In this study follow-up was limited to eight weeks and the number of participants was small and the

power of the study to compare what appear to be two effective treatments for CTS may have been limited.

Although this review focuses on comparison of local CTS injection to non-surgical interventions, it is necessary to consider local steroid injection in relation to the common intervention of surgical decompression. Ly-Pen et al (Ly-Pen 2005) demonstrated in a prospective, randomized open one year trial that persons receiving local corticosteroid injection had better short term outcomes and similar one year outcomes compared to surgical decompression.

Definition of participants

Few of the included studies provided an explicit definition of CTS such as that provided by the American Association of Neurology (AAN 1993), although except for Ozdogan (Ozdogan 1984) all used electrodiagnostic studies in conjunction with clinical symptoms. The clinical outcome for five of these studies (Armstrong 2004; Dammers 1999; Lucantoni 1992; O'Gradaigh 2000; Ozdogan 1984) was also loosely defined using a subjective ordinal ranking scale. Neither the magnitude of improvement using these scales nor the changes in specific symptoms are clear. The studies by Wong (Wong 2001; Wong 2005), Sevim (Sevim 2004), Gokoglu (Gokoglu 2005), Aygul (Aygul 2005) and Celiker (Celiker 2002) each used validated symptom scales. The severity of CTS in the study by Dammers (Dammers 1999) would be considered severe for most subjects since 80% of all participants had absent sensory nerve action potentials on nerve conduction studies. The other studies did not report severity of CTS other than to indicate that findings such as thenar atrophy would lead to exclusion from the study. Participants in each of the studies by Dammers (Dammers 1999) and Ozdogan (Ozdogan 1984) had had symptoms for a mean of between two to four years. The average duration of symptoms for the study by Celiker (Celiker 2002) was between six to nine months. The duration of symptoms were not reported by Wong or Lucantoni. Therefore, it remains unclear as to which population, based on severity and duration of symptoms, is most responsive to local corticosteroid injection. Gelberman (Gelberman 1980), in a prospective trial of corticosteroid injection, identified that participants with milder CTS severity (based on both symptoms and nerve conduction studies) had more symptomatic relief and duration of effectiveness of treatment compared to persons with severe CTS.

Different types, routes and doses

Although the included studies each used different injection techniques and dosages, no particular dosage or type of medication provided a clearly superior outcome. The lowest dosage and relative potency used for injection in the studies reviewed was 15 mg of prednisolone (Wong 2001) compared to 40 mg of methylprednisolone used in other studies (Celiker 2002; Dammers 1999; Lucantoni 1992) and there was still benefit identified at this lower dosage three months after injection when compared to oral corticosteroid. The fact that the studies of Dammers (Dammers 1999), Ozdogan (Ozdogan 1984) and Wong (Wong 2001) showed a significant benefit compared to control interventions, despite differences in type and potency of injectable corticosteroids, patient populations and settings, lends support to the generalizability of these results for treatment of CTS. Sevim et al (Sevim 2004) compared distal versus proximal local corticosteroid injection of the carpal tunnel and found no significant difference in outcome. However, an important limitation of this study was the prolonged period of time between injection and outcome assessment at approximately 11 months, where as noted above there is controversy with regards to the expected duration of benefit. Two low quality studies (Habib 2006; O'Gradaigh 2000) did not show benefit of higher dosage versus lower dosage of corticosteroid injection. Similarly O'Gradaigh (O'Gradaigh 2000) did not show any benefit of longer acting corticosteroids over shorter duration corticosteroids for injection. Similar to this finding is the high quality study provided by Wong et al. (Wong 2005) that did not demonstrate significant clinical improvement following two injections of local corticosteroid compared to just one injection.

Two important characteristics of an intervention include adverse outcomes associated with the intervention as well as the cost effectiveness of the intervention. These elements were not specifically examined for this review, but will be included in future updates.

AUTHORS' CONCLUSIONS

Implications for practice

Local corticosteroid injection for severe CTS provides symptomatic benefit at one month compared to placebo. The duration of benefit and the effect on mild and moderate CTS are not known, but the effects appear to be time limited and benefit beyond one month remains uncertain. Local corticosteroid injection provides more improvement in symptoms than oral corticosteroid for up to three months. Compared to a single systemic injection, local corticosteroid injection provides clinical improvement in symptoms at one month. The symptom improvement with local corticosteroid is not significantly different from anti-inflammatory medication and neutral angle wrist splinting at eight weeks after onset of treatment. Two injections of corticosteroid into the carpal tunnel do not provide further clinical benefit compared to one injection.

Implications for research

Research is required to determine the duration of benefit from local corticosteroid injection and to identify candidates for treatment based on severity and duration of symptoms. Local corticosteroid injection should also be compared to, and combined with, other non-surgical and even surgical interventions to determine the optimum management of CTS.

FEEDBACK

Comment

Summary

Sender: Hans Dammers
Contact: hans.dammers@hetnet.nl
Date: 17 February 2002

The authors of the BMJ study on local corticosteroid injection for carpal tunnel syndrome (Dammers 1999) have read your review and are disappointed. The review states that 'symptom relief beyond one month compared to placebo has not been demonstrated'. In the 'Discussion' you mention that blinding was broken in the placebo group after one month. For the greater part of the placebo group this was true, only because the protocol ordered it because an endpoint was scored blindly. Only after all the information was gathered and decisions had been made was blinding broken. Twenty four patients did not experience benefit, six did have a benefit, but after three months in four patients complaints returned. Only in these cases was blinding broken. The authors of this review and Hayward (Hayward 2000) in his comment on our paper expected more spontaneous recoveries, but our patients had an average duration of carpal tunnel syndrome of twenty four months. It would be naive to expect spontaneous recoveries after such a long time and it is probably not ethical as well to keep patients off treatment for any longer. Fifty per cent of the patients in the treatment group as well as 50% of the non -responders in the placebo group which received the same dose of methylprednisolone had a benefit when followed for a year.

We have just finished a second study where patients could make a choice for surgery or a second injection, after the effect of the first injection was gone. After two injections, only 24.6% asked for surgery after 12 months.

We regret you have made a mistake by stating that the effect of an injection close to the carpal tunnel only provides improvement for one month. The authors of this study are eager to hear your comments.

Author's reply

Date: May 14 2002

We are responding to the comment provided by H. Dammers with regards to our Systematic Review entitled 'Local corticosteroid injection for carpal tunnel syndrome' (Marshall 2000).

Dr Hans Dammers, the principle author of the paper entitled 'Injection with methylprednisolone proximal to the carpal tunnel: randomized double blind trial' (Dammers 1999) disagrees with the conclusions reached in our systematic review specifically with regards to interpretation of their manuscript.

Dammers et al. admit that for the placebo group the blinding was 'broken for the greater part' at one month post injection (this represents 80% of the group). By 3 months follow-up 93% (28 out of 30) of the placebo group was unblinded. We agree that this study clearly demonstrates after one month that local corticosteroid injection is effective for CTS. However, we do not agree that this study provides good evidence of benefit beyond this point. First of all, this study is contrary to most studies that suggest benefit of local corticosteroid injection is of limited duration (Girlanda 1993; Giannini 1991; Gelberman 1980; Weiss 1994). For this study, at one month 50% of (total) patients had been unblinded whereas 65% of patients had been unblinded at 3 months, and bias was likely to have been high for two reasons. First, the investigators would likely have realized that most patients receiving placebo injection had not responded and had proceeded to a second active injection. Second, local corticosteroid has limited expected duration and spontaneous recovery (addressed below) does often occur for CTS. Given this, with 80% of the placebo group removed from follow-up in this study, no meaningful comparison was possible beyond one month for the effect of local corticosteroid injection.

We also suggest that this study had further bias in that the two groups, active and placebo were treated differently. The placebo group was offered local injection with methylprednisolone after blinding was broken whereas the patients in the intervention group were offered surgery directly. Based on the comment that 'it is probably not ethical to keep patients off treatment any longer', we would question the clinical equipoise on which this study was based. If the authors believed that local corticosteroid injection was truly beneficial and they were concerned after one month that treatment was being withheld, why would another treatment not have been offered in conjunction with or instead of placebo injection? By the study design offering differential management to the placebo versus control group, the authors suggest that they are "certain" that local steroid injection is effective. For the follow-up of patients beyond one month post injection we believe that the information presented by Dammers et al. is essentially equivalent to an open label, non-randomized study. Beyond one month, the majority of placebo injection patients are openly treated and the active treatment group was likely to have been suspected on the part of the examiners therefore bias potential at this point was very high.

With regards to the comment that 'it would be naïve to expect spontaneous recoveries after such a long time' again we do not necessarily agree. Although the authors indicate that the average duration of symptoms for patients was 25 months in the placebo group, in their protocol they accepted patients with symptoms of greater than 3 months and we are unable to get a good sense of the duration of symptoms since standard deviations were not provided. Further, when the paper by Dammers et al. was written in 1999, Futami et al . had previously published a paper in 1997 (Futami 1997) suggesting that 34% of CTS cases have spontaneous complete resolution of symptoms and that this generally occurs over a five month time frame. More recently, Padua et al (Padua 2001) have completed a multicentred Italian based study

that followed untreated carpal tunnel syndrome. These authors found that for patients with severe and moderate CTS there was spontaneous improvement in symptoms of 49% and 31% respectively.

We are unable to comment with regards to the findings of the second study by Dammers et al. that is referred to in the criticism since we have not reviewed the manuscript.

Although we believe that Dammers et al. have provided very good evidence for effectiveness of local corticosteroid injection for CTS up to one month post injection, for the above stated reasons, we do not believe that these results provide good evidence for effect beyond 1 month.

Shawn Marshall, Gaetan Tardif, Nigel Ashworth

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Contributors

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POTENTIAL CONFLICT OF INTEREST

None

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Armstrong 2004**
Methods	Randomized double-blind placebo controlled trial
Participants	Clinical diagnosis confirmed with NCS n = 81
Interventions	Group 1: 1 ml 1% lidocaine and 6 mg betamethasone suspension n = 43 Group 2: 1 ml 1% lidocaine and 1 ml saline (placebo) n = 36 Drop-outs n = 2
Outcomes	Primary: patient satisfaction with outcome of treatment Secondary: repeat NCS, readministration of CTS Functional Status and Symptom Severity questionnaires
Notes	
Allocation concealment	A – Adequate

Study	**Aygul 2005**
Methods	Randomized, unblinded, controlled trial

Characteristics of included studies (*Continued*)

Participants	Clinical diagnosis based on American Academy of Neurology criteria and mild to moderate CTS based on electrodiagnostic findings. Symptoms greater than 3 months. Injection group: n = 12; Iontophoresis group: n = 9; phonophoresis group n = 10
Interventions	Local corticosteroid injection group: 1 ml of dexamethasone sodium phosphate into the carpal tunnel; Iontophoresis group: 0.1% dexamethasone sodium phosphate applied locally with 1 to 4 mA current for 10 minutes, 5 days a week for 3 weeks; Phonophoresis group: Administered at 3 MHz and intensity of 1.0 W/cm2; 0.1% dexamethasone sodium phosphate solution for 10 minutes, 5 days a week for 3 weeks
Outcomes	NCS; Boston Carpal Tunnel questionnaire with the Symptom Severity and Functional Severity scores
Notes	
Allocation concealment	C – Inadequate

Study	**Celiker 2002**
Methods	Prospective, unblinded, randomized controlled trial
Participants	Clinical diagnosis confirmed with electrodiagnostic studies; Corticosteroid injection group n = 12; Splinting and antiinflammatory group n = 11
Interventions	Group A: Nocturnal neutral angle wrist splint and acemetacine 120 mg/day; Group B: Local carpal tunnel injection with 40 mg methylprednisolone acetate
Outcomes	Symptom Severity Score at 2 and 8 weeks; VAS at 2 and 8 weeks; Tinel sign and Phalen's test at 8 weeks; Peripheral nerve conduction studies
Notes	
Allocation concealment	A – Adequate

Study	**Dammers 1999**
Methods	Randomized double blind placebo controlled trial
Participants	Symptoms greater than 3 months confirmed with electrophysiological studies; n = 60; Intervention group (n = 30); Control Group (n = 30); 50 females 10 males
Interventions	Injection of 10 mg lignocaine or 10 mg lignocaine and 40 mg methylprednisolone proximal to the carpal tunnel
Outcomes	Symptom improvement defined as no symptoms or only minor symptoms where patient indicated no further treatment was required
Notes	Study stopped early due to proven effectiveness of intervention (decision to stop made after review of 40 participants but in interim another 20 had been recruited for the study); 25/30 in active and 23/30 in placebo group had absent sensory nerve action potentials
Allocation concealment	A – Adequate

Study	**Gokoglu 2005**
Methods	Randomized, unblinded, controlled trial
Participants	Clinical diagnosis of CTS confirmed with electrodiagnostic studies. Local corticosteroid injection group; n = 15; Iontophoresis group; n = 15
Interventions	Local corticosteroid injection group: 40 mg of methylprednisolone acetate (1 ml) injected locally in carpal tunnel;

Characteristics of included studies (*Continued*)

	Iontophoresis group: 0.4% dexamethasone sodium phosphate solution was used for iontophoresis where sessions lasted for 20 minutes and were administered every other day for 1 week.
Outcomes	Clinical examination, the Symptom Severity Scale and the Functional Severity Scale
Notes	
Allocation concealment	C – Inadequate

Study	**Habib 2006**
Methods	Randomized, unblinded, controlled trial
Participants	Symptoms of CTS for less than 1 year confirmed with electrodiagnostic studies. Classic injection approach at wrist crease n = 21; Injection using distal approach to carpal tunnel n = 21.
Interventions	Group 1: Classic injection approach at wrist crease with 35 mg methylprednisolone acetate mixed with 0.5 ml of 2% lidocaine. Group 2 was injected 2 to 3 cm in the middle distal to the wrist crease using a 29 guage, 1 ml insulin syringe. 15 mg of methylprednisolone and 0.15 ml 2% lidocaine was injected. Both groups had application of ethyl chloride spray prior to injection
Outcomes	Subjective symptom improvement, pain rating of injection technique on visual analog scale, and complications of injection procedure.
Notes	
Allocation concealment	C – Inadequate

Study	**Lucantoni 1992**
Methods	Randomized, unblinded, controlled trial
Participants	Clinical diagnosis confirmed with electrodiagnostic studies; n = 40; Corticosteroid injection n = 20; He-Ne laser n = 20
Interventions	Group 1: Local corticosteroid injection x 2 10 days apart Methylprednisolone 20 mg per injection; Group 2: Helium-Neon Laser at 3000 Hz; daily for an unstated number of days, for 20 minute sessions
Outcomes	Symptom improvement at 20 days and 6 months; NCS at 20 days and 6 months
Notes	
Allocation concealment	B – Unclear

Study	**O'Gradaigh 2000**
Methods	Randomized, single blind, controlled trial
Participants	Positive NCS or positive Phalen and Tinel test together with classic symptoms n = 64 (randomized participants)
Interventions	Phase 1 (low vs high dose): Group A: 25 mg hydrocortisone Group B: 100 mg hydrocortisone Group C: control/no injection Phase 2 (short vs long acting): Group D: 20 mg triamcinolone hexacetonide Group E: 100 mg hydrocortisone
Outcomes	Primary: Subjective change in symptoms on a five point scale Secondary: changes in NCS data, Phalen or Tinel test changes
Notes	

Characteristics of included studies (*Continued*)

Allocation concealment	C – Inadequate

Study	**Ozdogan 1984**
Methods	Randomized double blind placebo controlled trial
Participants	Clinical diagnosis; n = 37 Local injection group n = 18; Systemic / control injection group (n = 19); All females
Interventions	Carpal tunnel injection or intramuscular injection (ipsilateral deltoid muscle) of 1.5 mg betamethasone. Placebo was an equal volume of saline
Outcomes	Subjective clinical rating of symptoms
Notes	
Allocation concealment	C – Inadequate

Study	**Sevim 2004**
Methods	Randomized single blind controlled trial
Participants	Clinical symptoms of CTS confirmed with electrodiagnostic studies n = 120; Proximal injection group: n = 30; Distal injection group: n = 30; Splint group: n = 60
Interventions	Proximal injection group: injected volar surface 4 cm proximal to wrist crease; Distal Injection group: Injected volar surface at the anterior wrist flexion crease; Each group injected with 3 mg betamethasone disodium phosphate and 3 mg betamethasone acetate solution and 0.5cc 2% lidocaine HCL solution Splint group: standard neutral angle wrist splint worn nightly throughout study
Outcomes	Neurologic symptom score, Mean antidromic median sensory nerve conduction velocity, median versus ulnar digit IV antidromic sensory distal latency difference, median second lumbrical versus ulnar interossei distal motor latency difference
Notes	Not able to include data for splint groups since data provided in publication does not follow intent to treat and provides group assignments based on study compliance.
Allocation concealment	C – Inadequate

Study	**Wong 2001**
Methods	Randomized double blind placebo controlled trial
Participants	Clinical symptoms confirmed with electrodiagnostic studies and failed trial of splinting for 2 months
Interventions	Group 1: Local corticosteroid injection 15 mg prednisolone and daily oral placebo; Group 2: oral prednisolone 25 mg daily for 10 days and placebo local carpal tunnel injection
Outcomes	Global symptom score at 2, 8 and 12 weeks
Notes	
Allocation concealment	A – Adequate

Study	**Wong 2005**
Methods	Randomized double blind controlled trial

Participants	Clinical symptoms of CTS confirmed with electrodiagnostic tests and who had failed splinting treatment after 2 months. n = 40; Single injection group: n = 20 (17 females; 3 males) Double injection group: n = 20 (17 females/ 3 males)
Interventions	Both groups injected with 15 mg methylprednisolone into carpal tunnel. After 8 weeks double injection group received repeat injection with 15 mg methylprednisolone and the single injection group received an equal volume of saline solution (placebo).
Outcomes	Global symptom score at 8, 24 and 40 weeks post injection. Secondary outcomes included grip strength and median nerve distal mean latency values
Notes	Data for the main outcome of Global Symptom Score from Figure 1 and Table 2 is reversed for the groups. Data from Table 2 used for data entry for review.
Allocation concealment	C – Inadequate

Characteristics of excluded studies

Study	Reason for exclusion
Agarwal 2005	Study was a prospective non-randomized trial with no control group evaluating the effect of local corticosteroid in the management of mild CTS.
Dammers 2001	Published abstract. Brief summary of results reported.
Elbaz 1994	Published abstract only. Brief summary of results reported. Attempts made to contact for raw data.
Girlanda 1993	The authors did not report individual participant or actual numbers of patients who improved with treatment. Only statistical values were reported. Attempts to contact the authors were unsuccessful. The treatment intervention was different than usual since the carpal tunnel injection was carried out at baseline and repeated one week later for all participants.
Graham 2003	Study was a prospective non-randomized trial evaluating the effect of local steroid injection and wrist splinting.
Hagebeuk 2004	Study was a prospective uncontrolled study where all participants received local steroid injection. Emphasis of study was on change in electrophysiologic parameters.
Hui 2005	Study is a randomized controlled trial comparing local corticosteroid injection to surgical decompression for carpal tunnel syndrome. Study was excluded since it falls outside of the objectives of this review. More appropriate for the Cochrane review by Verdugo (2003) comparing surgical and non-surgical interventions for management of CTS.
Ly-Pen 2005	Study is a randomized controlled trial comparing local corticosteroid injection to surgical decompression for carpal tunnel syndrome. Study was excluded since it falls outside of the objectives of this review. More appropriate for the Cochrane review by Verdugo (2003) comparing surgical and non-surgical interventions for management of CTS.
Piotrowski 1998	Carpal tunnel injection was not the focus of the study. Only 25 of 158 injections were for CTS and outcome was primarily focussed on irritative reaction to injection.
Wu 1991	Blinded, randomized, controlled trial studying non-surgical intervention in CTS including local carpal tunnel corticosteroid injection, wrist splinting, vitamin B6, vitamin B12 and combined therapy. The study was excluded since a clinical outcome measure was not used and only peripheral nerve conduction studies were used as an outcome measure. The authors comment that other studies have relied on subjective patient report for effectiveness of intervention and that in this study the results are wholly based on objective electrophysiologic measures.

ADDITIONAL TABLES

Table 01. Electronic search strategies

MEDLINE	EMBASE	CINAHL
1 clinical trial.pt.	1 Clinical trial/	1 Clinical trial/
2 randomized controlled trial.pt.	2 Randomized controlled trial/	2 Randomized controlled trial/
3 tu.fs.	3 Randomization/	3 Randomization/
4 dt.fs.	4 Single blind procedure/	4 Single blind procedure/
5 random$.tw.	5 Double blind procedure/	5 Double blind procedure/
6 (double and blind$).tw.	6 Crossover procedure/	6 Crossover procedure/
7 placebo$.tw.	7 Placebo/	7 Placebo/
8 exp Comparative Study/	8 Randomi?ed controlled trial$.tw.	8 Randomi?ed controlled trial$.tw.
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	9 Rct.tw.	9 Rct.tw.
10 exp Carpal tunnel syndrome/ 11 exp Steroids/	10 (allocat$ adj2 random$).tw.	10 (allocat$ adj2 random$).tw.
12 exp injections/ or exp injections, intra-articular/	11 Single blind.tw.	11 Single blind.tw.
13 11 or 12	12 Double blind.tw.	12 Double blind.tw.
14 10 and 13	13 ((treble or triple) adj blind$).tw.	13 ((treble or triple) adj blind$).tw.
15 9 and 14	14 Placebo$.tw.	14 Placebo$.tw.
	15 Prospective study/	15 Prospective study/
	16 or/1-15	16 or/1-15
	17 Carpal tunnel syndrome/	17 Carpal tunnel syndrome/
	18 (carpal$ adj3 tunnel$).tw.	18 (carpal$ adj3 tunnel$).tw.
	19 cts.tw.	19 cts.tw.
	20 or/17-19	20 or/17-19
	21 16 and 20	21 16 and 20
	22 exp steroid/	22 exp steroid/
	23 exp corticosteroid/	23 exp corticosteroid/
	24 injection/	24 injection/
	25 intraarticular drug administration/	25 intraarticular drug administration/
	26 injection$.tw.	26 injection$.tw.
	27 (steroid$ or corticosteroid$).tw.	27 (steroid$ or corticosteroid$).tw.
	28 triamcinolone.tw.	28 triamcinolone.tw.
	29 prednisone.tw.	29 prednisone.tw.
	30 prednisolone.tw.	30 prednisolone.tw.
	31 or/22-30	31 or/22-30
	32 21 and 31	

Table 02. Study Quality Rating Scores - Jadad Scale

Study	Randomized	Double Blind	With-drawal/drop outs	Method Ran-domisation	Method Blinding	Allocation Concealed	Total Score
Armstrong 2004	1	1	1	1	1	Adequate	5
Aygul 2005	1	0	1	0	0	Unclear	2
Celiker 2002	1	0	1	1	0	Adequate	3
Dammers 1999	1	1	1	1	1	Adequate	5

Table 02. Study Quality Rating Scores - Jadad Scale (*Continued*)

Study	Randomized	Double Blind	Withdrawal/drop outs	Method Randomisation	Method Blinding	Allocation Concealed	Total Score
Gokoglu 2005	1	0	0	0	0	Unclear	1
Habib 2006	1	0	1	0	0	Unclear	2
Lucantoni 1992	1	0	0	0	0	Unclear	1
O'Gradaigh 2000	1	0	0	0	0	Unclear	1
Ozdogan 1984	1	1	0	0	1	Unclear	3
Sevim 2004	1	0	0	0	1	Unclear	2
Wong 2001	1	1	1	1	1	Adequate	5
Wong 2005	1	1	1	0	1	Unclear	4

Table 03. Local corticosteroid injection versus phonophoresis (Aygul 2005)

Outcome	Injection n/N	Phonophoresis n/N	RR (fixed) 95% CI
Significant improvement in digit 4 sensory latency difference median and ulnar nerves			
8 weeks post treatment	13/20	6/18	1.95 (0.94, 4.04)
4 months post treatment	12/20	7/18	1.54 (0.78, 3.05)
Significant improvement in sensory latency difference between digit 2 (median) and digit 5 (ulnar) nerves			
8 weeks post treatment	13/20	7/18	1.67 (0.86, 3.24)
4 months post treatment	14/20	5/18	2.52 (1.13, 5.60)
Significant improvement in digit 2 (median) and digit 5 (ulnar) sensory nerve amplitude ratio			
8 weeks post treatment	8/20	4/18	1.80 (0.65, 4.98)
4 months post treatment	12/20	4/18	2.70 (1.06, 6.88)
Change in mean sensory distal latency			
8 weeks post treatment	7/20	5/18	1.26 (0.48, 3.27)
4 months post treatment	10/20	6/18	1.50 (0.68, 3.29)
Significant improvement in median sensory nerve conduction velocity			
8 weeks post treatment	4/20	2/18	1.80 (0.37, 8.68)

Table 03. Local corticosteroid injection versus phonophoresis (Aygul 2005) (*Continued*)

Outcome	Injection n/N	Phonophoresis n/N	RR (fixed) 95% CI
4 months post treatment	8/20	4/18	1.80 (0.65, 4.98)
Significant improvement in median nerve sensory amplitude potential			
8 weeks post treatment	5/20	1/18	4.50 (0.58, 34.97)
4 months post treatment	6/20	0/18	11.76 (0.71, 195.11)
Significant improvement in median nerve distal motor latency			
8 weeks post treatment	6/20	5/18	1.08 (0.40, 2.94)
4 months post treatment	7/20	6/18	1.05 (0.43, 2.54)
Significant improvement in median nerve motor conduction velocity			
8 weeks post treatment	2/20	0/18	4.52 (0.23, 88.38)
4 months post treatment	3/20	0/18	6.33 (0.35, 114.81)
Significant improvement in median nerve terminal latency index			
8 weeks post treatment	5/20	2/18	2.25 (0.50, 10.20)
4 months post treatment	5/20	3/18	1.50 (0.42, 5.41)

ANALYSES

Comparison 01. Effect of local corticosteroid injection at 1 month or less

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Clinical improvement	2	141	Relative Risk (Fixed) 95% CI	2.58 [1.72, 3.87]

Comparison 02. Local versus systemic steroids

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Clinical improvement Global Symptom Score			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
02 Clinical improvement at 1 month	1	37	Relative Risk (Fixed) 95% CI	3.17 [1.02, 9.87]

Comparison 03. Local corticosteroid injection versus oral antiinflammatory and splinting

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Symptom Severity Checklist score			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
02 Visual Analog Scale score			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
03 Phalen's test at 8 weeks	1	37	Relative Risk (Fixed) 95% CI	5.41 [0.30, 97.80]
04 Tinel's Sign at 8 weeks	1	37	Relative Risk (Fixed) 95% CI	2.29 [0.53, 9.86]
05 Change in Motor Distal Latency at 8 weeks	1	23	Weighted Mean Difference (Fixed) 95% CI	-0.10 [-0.72, 0.52]

06 Change in Sensory Distal Latency at 8 weeks	1	23	Weighted Mean Difference (Fixed) 95% CI	-0.10 [-0.60, 0.40]

Comparison 04. Local corticosteroid injection versus Helium-Neon Laser

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Symptom improvement at 20 days	1	40	Relative Risk (Fixed) 95% CI	1.89 [1.12, 3.17]
02 Change in sensory conduction velocity at 6 months	1	36	Weighted Mean Difference (Fixed) 95% CI	0.75 [-2.81, 4.31]

Comparison 05. High dose local corticosteroid versus low dose corticosteroid

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Clinical improvement			Relative Risk (Fixed) 95% CI	Subtotals only

Comparison 06. Short-acting versus long-acting local corticosteroid injection

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Clinical improvement at 6 weeks	1	39	Relative Risk (Fixed) 95% CI	1.08 [0.71, 1.64]

Comparison 07. Local corticosteroid injection versus iontophoresis

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Symptom severity score			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
02 Functional status score			Weighted Mean Difference (Random) 95% CI	Subtotals only
03 Pain Visual Analog Scale			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
04 Paresthesia 8 weeks post treatment	1	48	Relative Risk (Fixed) 95% CI	0.42 [0.13, 1.33]
05 Tinel sign 8 weeks post treatment	1	48	Relative Risk (Fixed) 95% CI	0.31 [0.08, 1.29]
06 Positive Phalen Test 8 weeks post treatment	1	48	Relative Risk (Fixed) 95% CI	0.35 [0.11, 1.08]
07 Reverse Phalen sign 8 weeks post treatment	1	48	Relative Risk (Fixed) 95% CI	0.35 [0.08, 1.48]
08 Numbness 8 weeks post treatment	1	48	Relative Risk (Fixed) 95% CI	0.56 [0.20, 1.53]
09 Significant improvement in median nerve sensory amplitude potential			Relative Risk (Fixed) 95% CI	Totals not selected
10 Significant improvement in median nerve distal motor latency			Relative Risk (Fixed) 95% CI	Totals not selected
11 Significant improvement in median nerve motor conduction velocity			Relative Risk (Fixed) 95% CI	Totals not selected

12 Significant improvement in median sensory nerve conduction velocity		Relative Risk (Fixed) 95% CI	Totals not selected
13 Significant improvement sensory latency difference between digit 2 (Median) and digit 5 (Ulnar)		Relative Risk (Fixed) 95% CI	Totals not selected
14 Significant improvement in digit 2 Median and digit 5 Ulnar sensory nerve amplitude ratio		Relative Risk (Fixed) 95% CI	Totals not selected
15 Change in mean sensory distal latency		Relative Risk (Fixed) 95% CI	Totals not selected
16 Significant improvement digit 4 sensory latency difference median and ulnar nerves		Relative Risk (Fixed) 95% CI	Totals not selected
17 Significant improvement in median nerve terminal latency index		Relative Risk (Fixed) 95% CI	Totals not selected

Comparison 08. Wrist crease versus distal to wrist crease local corticosteroid injection

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Clinical improvement			Relative Risk (Fixed) 95% CI	Totals not selected
02 Pain at injection site	1	42	Weighted Mean Difference (Fixed) 95% CI	-0.76 [-1.56, 0.04]

Comparison 09. Local corticosteroid injection versus phonophoresis

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Symptom Severity Scale post treatment			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
02 Functional Severity Score post treatment			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

Comparison 10. Single versus double local corticosteroid injection

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Global Symptom Score			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

Comparison 11. Wrist crease versus proximal to wrist crease local corticosteroid injection

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Neurologic Symptom Score 11 months	1	57	Weighted Mean Difference (Fixed) 95% CI	2.17 [-1.07, 5.41]
02 Mean antidromic median sensory conduction velocity digits I, II, III at 11 months	1	57	Weighted Mean Difference (Fixed) 95% CI	-1.01 [-3.72, 1.70]
03 Median versus ulnar digit IV antidromic sensory distal latency difference at 11 months	1	57	Weighted Mean Difference (Fixed) 95% CI	0.09 [-0.14, 0.32]

04 Median second lumbrical versus ulnar interossei distal motor latency difference at 11 months	1	57	Weighted Mean Difference (Fixed) 95% CI	0.13 [-0.12, 0.38]

INDEX TERMS

Medical Subject Headings (MeSH)

Anti-Inflammatory Agents [*administration & dosage]; Carpal Tunnel Syndrome [*drug therapy]; Injections, Intra-Articular; Iontophoresis; Phonophoresis; Randomized Controlled Trials as Topic; Steroids [administration & dosage]

MeSH check words

Humans

COVER SHEET

Title	Local corticosteroid injection for carpal tunnel syndrome
Authors	Marshall S, Tardif G, Ashworth N
Contribution of author(s)	Dr. Shawn Marshall is the primary author of this systematic review. He was involved in the review and evaluation of studies to be included as well as data entry, analysis and preparation of the manuscript. Dr. Tardif and Ashworth were involved in the selection and evaluation of studies to be included in the review and also participated in editing the review.
Issue protocol first published	1999/2
Review first published	2000/4
Date of most recent amendment	21 February 2007
Date of most recent SUBSTANTIVE amendment	20 February 2007
What's New	A search of the Cochrane Neuromuscular Disease Group Register was last undertaken in May 2006, MEDLINE (January 1966 to May 2006) and EMBASE (January 1980 to May 2006). These searches identified an additional 16 randomised controlled trials, 10 have been excluded and 3 are awaiting assessment. Three new studies have been included and the conclusions have been changed.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	Information not supplied by author
Date authors' conclusions section amended	Information not supplied by author
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DOI 10.1002/14651858.CD001554.pub2

Cochrane Library number CD001554

Editorial group Cochrane Neuromuscular Disease Group

Editorial group code HM-NEUROMUSC

GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Effect of local corticosteroid injection at 1 month or less, Outcome 01 Clinical improvement

Review: Local corticosteroid injection for carpal tunnel syndrome
Comparison: 01 Effect of local corticosteroid injection at 1 month or less
Outcome: 01 Clinical improvement

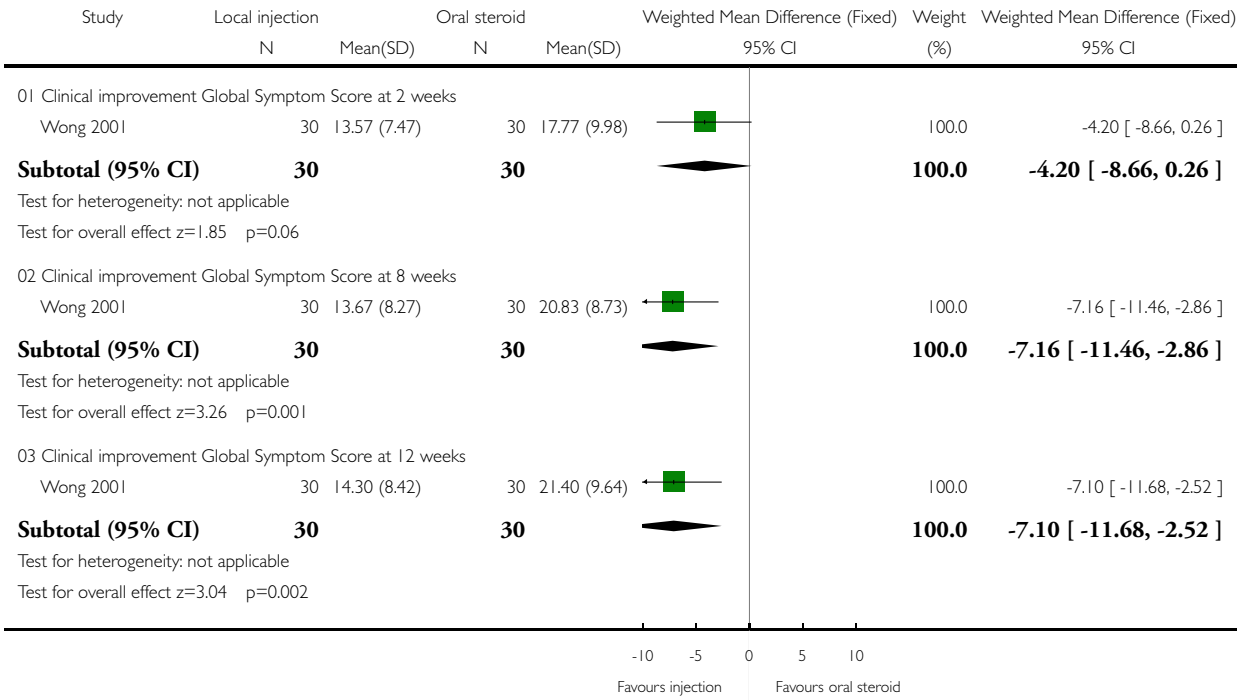
Study	Local injection n/N	Placebo n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Clinical improvement 2 weeks post injection					
Armstrong 2004	30/43	13/38		69.7	2.04 [1.26, 3.31]
Subtotal (95% CI)	**43**	**38**		**69.7**	**2.04 [1.26, 3.31]**
Total events: 30 (Local injection), 13 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.89 p=0.004					
02 Clinical improvement 1 month post injection					
Dammers 1999	23/30	6/30		30.3	3.83 [1.82, 8.05]
Subtotal (95% CI)	**30**	**30**		**30.3**	**3.83 [1.82, 8.05]**
Total events: 23 (Local injection), 6 (Placebo)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.55 p=0.0004					
Total (95% CI)	**73**	**68**		**100.0**	**2.58 [1.72, 3.87]**
Total events: 53 (Local injection), 19 (Placebo)					
Test for heterogeneity chi-square=2.01 df=1 p=0.16 I^2 =50.2%					
Test for overall effect z=4.59 p<0.00001					

Analysis 02.01. Comparison 02 Local versus systemic steroids, Outcome 01 Clinical improvement Global Symptom Score

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 02 Local versus systemic steroids

Outcome: 01 Clinical improvement Global Symptom Score

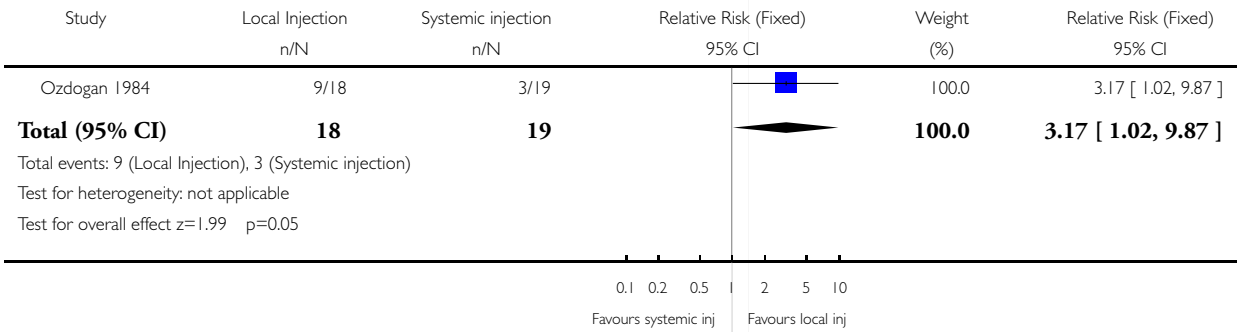


Analysis 02.02. Comparison 02 Local versus systemic steroids, Outcome 02 Clinical improvement at 1 month

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 02 Local versus systemic steroids

Outcome: 02 Clinical improvement at 1 month

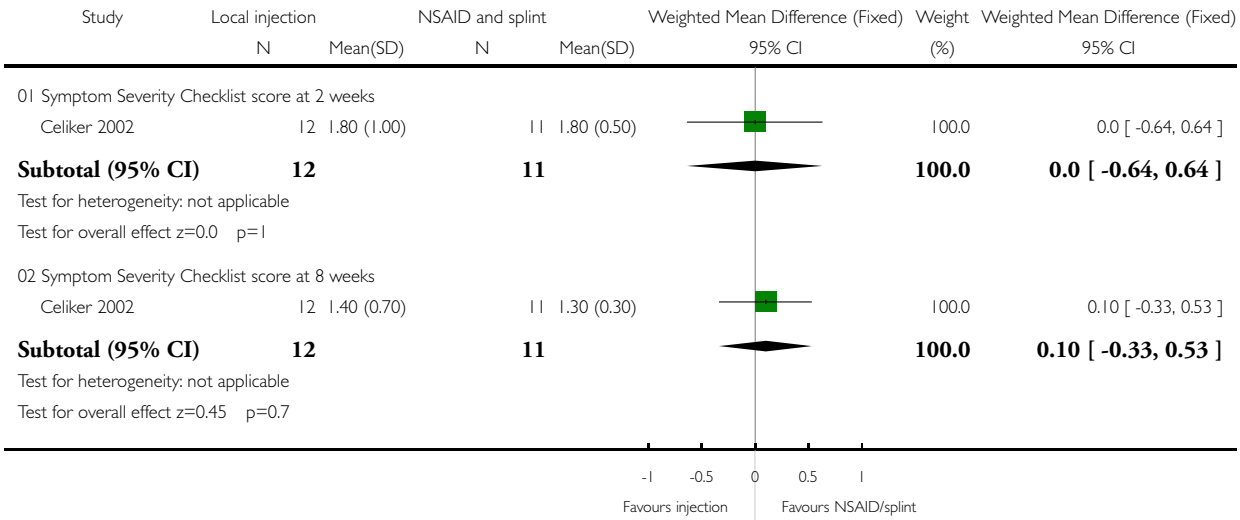


Analysis 03.01. Comparison 03 Local corticosteroid injection versus oral antiinflammatory and splinting, Outcome 01 Symptom Severity Checklist score

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 03 Local corticosteroid injection versus oral antiinflammatory and splinting

Outcome: 01 Symptom Severity Checklist score

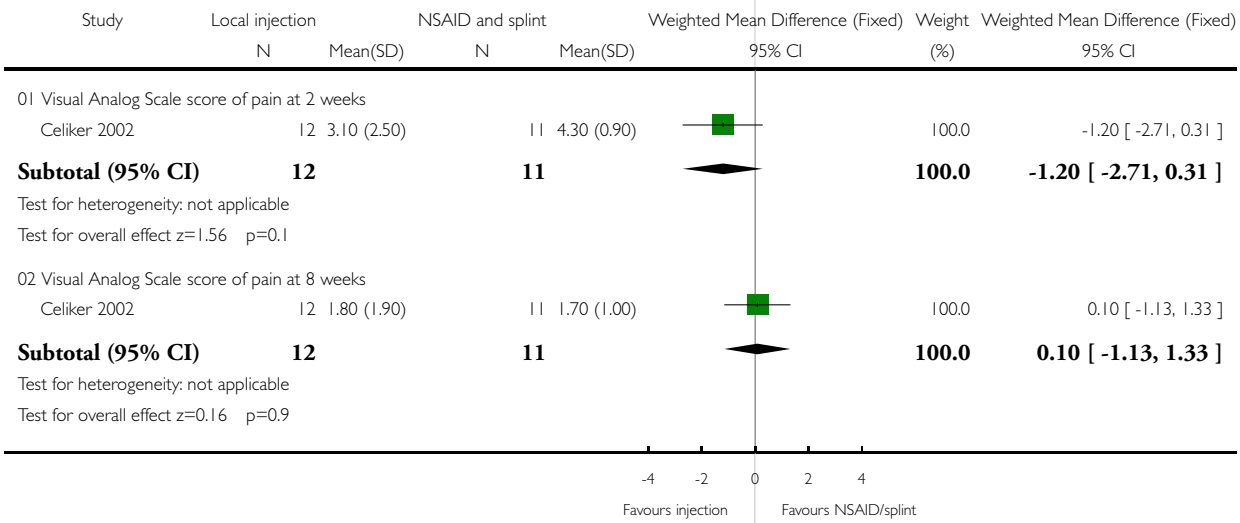


Analysis 03.02. Comparison 03 Local corticosteroid injection versus oral antiinflammatory and splinting, Outcome 02 Visual Analog Scale score

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 03 Local corticosteroid injection versus oral antiinflammatory and splinting

Outcome: 02 Visual Analog Scale score



Analysis 03.03. Comparison 03 Local corticosteroid injection versus oral antiinflammatory and splinting, Outcome 03 Phalen's test at 8 weeks

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 03 Local corticosteroid injection versus oral antiinflammatory and splinting

Outcome: 03 Phalen's test at 8 weeks

Study	Local injection n/N	NSAID and splint n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Celiker 2002	3/21	0/16		100.0	5.41 [0.30, 97.80]
Total (95% CI)	**21**	**16**		**100.0**	**5.41 [0.30, 97.80]**

Total events: 3 (Local injection), 0 (NSAID and splint)

Test for heterogeneity: not applicable

Test for overall effect z=1.14 p=0.3

Analysis 03.04. Comparison 03 Local corticosteroid injection versus oral antiinflammatory and splinting, Outcome 04 Tinel's Sign at 8 weeks

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 03 Local corticosteroid injection versus oral antiinflammatory and splinting

Outcome: 04 Tinel's Sign at 8 weeks

Study	Local injection n/N	NSAID and splint n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Celiker 2002	6/21	2/16		100.0	2.29 [0.53, 9.86]
Total (95% CI)	**21**	**16**		**100.0**	**2.29 [0.53, 9.86]**

Total events: 6 (Local injection), 2 (NSAID and splint)

Test for heterogeneity: not applicable

Test for overall effect z=1.11 p=0.3

Analysis 03.05. Comparison 03 Local corticosteroid injection versus oral antiinflammatory and splinting, Outcome 05 Change in Motor Distal Latency at 8 weeks

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 03 Local corticosteroid injection versus oral antiinflammatory and splinting

Outcome: 05 Change in Motor Distal Latency at 8 weeks

Study	Local injection N	Mean(SD)	NSAID and splint N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Celiker 2002	12	0.80 (0.70)	11	0.90 (0.80)		100.0	-0.10 [-0.72, 0.52]
Total (95% CI)	**12**		**11**			**100.0**	**-0.10 [-0.72, 0.52]**

Test for heterogeneity: not applicable

Test for overall effect z=0.32 p=0.8

Analysis 03.06. Comparison 03 Local corticosteroid injection versus oral antiinflammatory and splinting, Outcome 06 Change in Sensory Distal Latency at 8 weeks

Review: Local corticosteroid injection for carpal tunnel syndrome

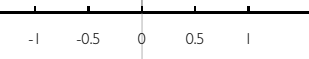
Comparison: 03 Local corticosteroid injection versus oral antiinflammatory and splinting

Outcome: 06 Change in Sensory Distal Latency at 8 weeks

Study	Local injection N	Mean(SD)	NSAID and splint N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Celiker 2002	12	0.50 (0.50)	11	0.60 (0.70)		100.0	-0.10 [-0.60, 0.40]
Total (95% CI)	**12**		**11**			**100.0**	**-0.10 [-0.60, 0.40]**

Test for heterogeneity: not applicable

Test for overall effect z=0.39 p=0.7



Analysis 04.01. Comparison 04 Local corticosteroid injection versus Helium-Neon Laser, Outcome 01 Symptom improvement at 20 days

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 04 Local corticosteroid injection versus Helium-Neon Laser

Outcome: 01 Symptom improvement at 20 days

Study	Local injection n/N	He-Ne Laser n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Lucantoni 1992	17/20	9/20		100.0	1.89 [1.12, 3.17]
Total (95% CI)	**20**	**20**		**100.0**	**1.89 [1.12, 3.17]**

Total events: 17 (Local injection), 9 (He-Ne Laser)

Test for heterogeneity: not applicable

Test for overall effect z=2.40 p=0.02

Analysis 04.02. Comparison 04 Local corticosteroid injection versus Helium-Neon Laser, Outcome 02 Change in sensory conduction velocity at 6 months

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 04 Local corticosteroid injection versus Helium-Neon Laser

Outcome: 02 Change in sensory conduction velocity at 6 months

Study	Local injection N	Mean(SD)	He-Ne Laser N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Lucantoni 1992	19	35.32 (5.02)	17	34.57 (5.80)		100.0	0.75 [-2.81, 4.31]
Total (95% CI)	**19**		**17**			**100.0**	**0.75 [-2.81, 4.31]**

Test for heterogeneity: not applicable

Test for overall effect z=0.41 p=0.7

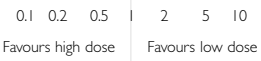
Analysis 05.01. Comparison 05 High dose local corticosteroid versus low dose corticosteroid, Outcome 01 Clinical improvement

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 05 High dose local corticosteroid versus low dose corticosteroid

Outcome: 01 Clinical improvement

Study	Low dose n/N	High dose n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Clinical improvement at 1 week					
Habib 2006	21/21	21/21		0.0	Not estimable
Subtotal (95% CI)	**21**	**21**		**0.0**	**Not estimable**
Total events: 21 (Low dose), 21 (High dose)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
02 Clinical improvement at 3 weeks					
Habib 2006	15/21	17/21		100.0	0.88 [0.63, 1.24]
Subtotal (95% CI)	**21**	**21**		**100.0**	**0.88 [0.63, 1.24]**
Total events: 15 (Low dose), 17 (High dose)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.72 p=0.5					
03 Clinical improvement at 6 weeks					
Habib 2006	14/21	15/21		42.9	0.93 [0.62, 1.40]
O'Gradaigh 2000	21/32	20/32		57.1	1.05 [0.73, 1.52]
Subtotal (95% CI)	**53**	**53**		**100.0**	**1.00 [0.76, 1.31]**
Total events: 35 (Low dose), 35 (High dose)					
Test for heterogeneity chi-square=0.18 df=1 p=0.67 I^2 =0.0%					
Test for overall effect z=0.0 p=1					
04 Clinical improvement at 12 weeks					
Habib 2006	12/21	12/21		100.0	1.00 [0.59, 1.69]
Subtotal (95% CI)	**21**	**21**		**100.0**	**1.00 [0.59, 1.69]**
Total events: 12 (Low dose), 12 (High dose)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.0 p=1					



Analysis 06.01. Comparison 06 Short-acting versus long-acting local corticosteroid injection, Outcome 01 Clinical improvement at 6 weeks

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 06 Short-acting versus long-acting local corticosteroid injection

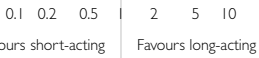
Outcome: 01 Clinical improvement at 6 weeks

Study	Short-acting n/N	Long-acting n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
O'Gradaigh 2000	13/18	14/21		100.0	1.08 [0.71, 1.64]
Total (95% CI)	**18**	**21**		**100.0**	**1.08 [0.71, 1.64]**

Total events: 13 (Short-acting), 14 (Long-acting)

Test for heterogeneity: not applicable

Test for overall effect z=0.38 p=0.7



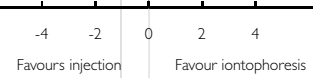
Analysis 07.01. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 01 Symptom severity score

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 01 Symptom severity score

Study	Injection N	Mean(SD)	Iontophoresis N	Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 Symptom severity score 2 weeks post treatment							
Gokoglu 2005	15	1.90 (0.70)	15	2.50 (0.90)		100.0	-0.60 [-1.18, -0.02]
Subtotal (95% CI)	**15**		**15**			**100.0**	**-0.60 [-1.18, -0.02]**
Test for heterogeneity: not applicable							
Test for overall effect z=2.04 p=0.04							
02 Symptom severity score 8 weeks post treatment							
Aygul 2005	12	1.37 (0.49)	9	1.51 (0.46)		67.6	-0.14 [-0.55, 0.27]
Gokoglu 2005	15	1.60 (0.60)	15	2.20 (1.00)		32.4	-0.60 [-1.19, -0.01]
Subtotal (95% CI)	**27**		**24**			**100.0**	**-0.29 [-0.63, 0.05]**
Test for heterogeneity chi-square=1.58 df=1 p=0.21 I^2 =36.6%							
Test for overall effect z=1.69 p=0.09							
03 Symptom severity score 4 months post treatment							
Aygul 2005	12	1.47 (0.52)	9	2.07 (0.91)		100.0	-0.60 [-1.26, 0.06]
Subtotal (95% CI)	**12**		**9**			**100.0**	**-0.60 [-1.26, 0.06]**
Test for heterogeneity: not applicable							
Test for overall effect z=1.77 p=0.08							

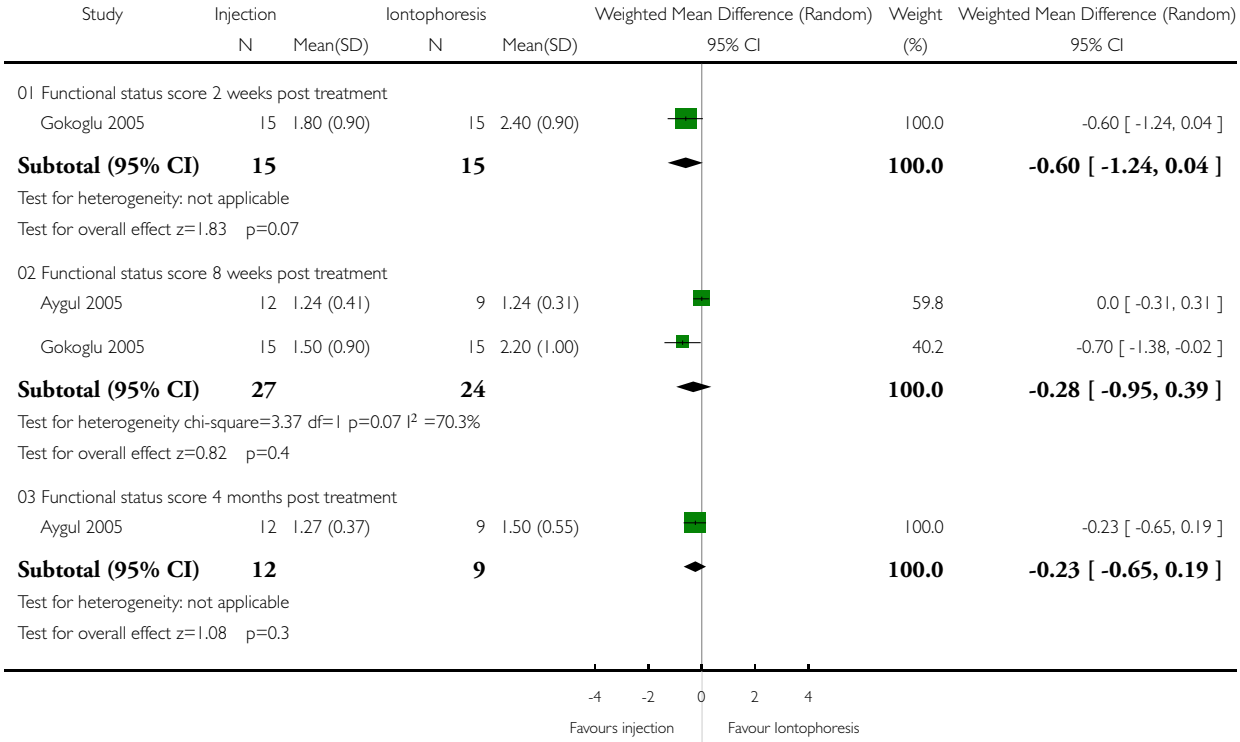


Analysis 07.02. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 02 Functional status score

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 02 Functional status score

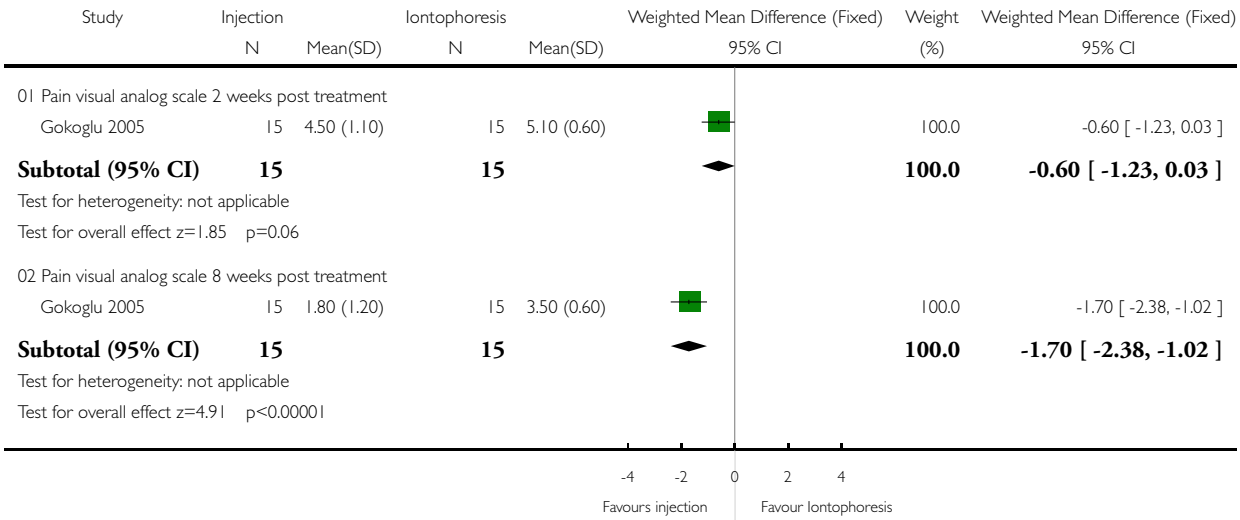


Analysis 07.03. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 03 Pain Visual Analog Scale

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 03 Pain Visual Analog Scale

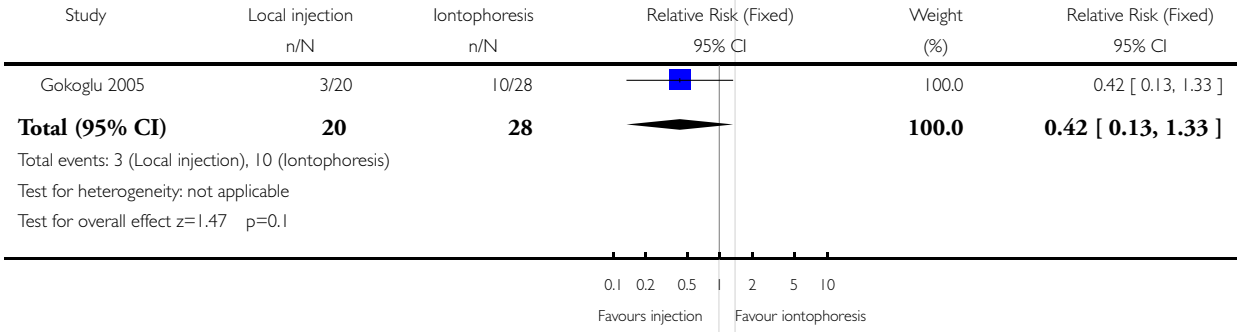


Analysis 07.04. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 04 Paresthesia 8 weeks post treatment

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 04 Paresthesia 8 weeks post treatment



Analysis 07.05. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 05 Tinel sign 8 weeks post treatment

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 05 Tinel sign 8 weeks post treatment

Study	Local injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gokoglu 2005	2/20	9/28		100.0	0.31 [0.08, 1.29]
Total (95% CI)	**20**	**28**		**100.0**	**0.31 [0.08, 1.29]**

Total events: 2 (Local injection), 9 (Iontophoresis)

Test for heterogeneity: not applicable

Test for overall effect z=1.61 p=0.1

Analysis 07.06. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 06 Positive Phalen Test 8 weeks post treatment

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 06 Positive Phalen Test 8 weeks post treatment

Study	Local injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gokoglu 2005	3/20	12/28		100.0	0.35 [0.11, 1.08]
Total (95% CI)	**20**	**28**		**100.0**	**0.35 [0.11, 1.08]**

Total events: 3 (Local injection), 12 (Iontophoresis)

Test for heterogeneity: not applicable

Test for overall effect z=1.82 p=0.07

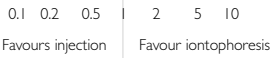
Analysis 07.07. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 07 Reverse Phalen sign 8 weeks post treatment

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 07 Reverse Phalen sign 8 weeks post treatment

Study	Local injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gokoglu 2005	2/20	8/28		100.0	0.35 [0.08, 1.48]
Total (95% CI)	**20**	**28**		**100.0**	**0.35 [0.08, 1.48]**
Total events: 2 (Local injection), 8 (Iontophoresis)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.43 p=0.2					



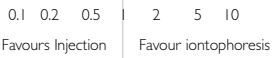
Analysis 07.08. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 08 Numbness 8 weeks post treatment

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 08 Numbness 8 weeks post treatment

Study	Local injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Gokoglu 2005	4/20	10/28		100.0	0.56 [0.20, 1.53]
Total (95% CI)	**20**	**28**		**100.0**	**0.56 [0.20, 1.53]**
Total events: 4 (Local injection), 10 (Iontophoresis)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.13 p=0.3					



Analysis 07.09. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 09 Significant improvement in median nerve sensory amplitude potential

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 09 Significant improvement in median nerve sensory amplitude potential

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	5/20	2/18		2.25 [0.50, 10.20]
02 4 months post treatment				
Aygul 2005	6/20	2/18		2.70 [0.62, 11.72]

Analysis 07.10. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 10 Significant improvement in median nerve distal motor latency

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 10 Significant improvement in median nerve distal motor latency

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	6/20	5/18		1.08 [0.40, 2.94]
02 4 months post treatment				
Aygul 2005	7/20	1/18		6.30 [0.86, 46.37]

Analysis 07.11. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 11 Significant improvement in median nerve motor conduction velocity

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 11 Significant improvement in median nerve motor conduction velocity

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	2/20	0/18		4.52 [0.23, 88.38]
02 4 months post treatment				
Aygul 2005	3/20	2/18		1.35 [0.25, 7.19]

Analysis 07.12. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 12 Significant improvement in median sensory nerve conduction velocity

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 12 Significant improvement in median sensory nerve conduction velocity

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	4/20	2/18		1.80 [0.37, 8.68]
02 4 months post treatment				
Aygul 2005	8/20	3/18		2.40 [0.75, 7.69]

Analysis 07.13. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 13 Significant improvement sensory latency difference between digit 2 (Median) and digit 5 (Ulnar)

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 13 Significant improvement sensory latency difference between digit 2 (Median) and digit 5 (Ulnar)

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	13/20	4/18		2.93 [1.16, 7.36]
02 4 months post treatment				
Aygul 2005	14/20	5/18		2.52 [1.13, 5.60]

Analysis 07.14. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 14 Significant improvement in digit 2 Median and digit 5 Ulnar sensory nerve amplitude ratio

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 14 Significant improvement in digit 2 Median and digit 5 Ulnar sensory nerve amplitude ratio

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	8/20	3/18		2.40 [0.75, 7.69]
02 4 months post treatment				
Aygul 2005	12/20	4/18		2.70 [1.06, 6.88]

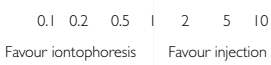
Analysis 07.15. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 15 Change in mean sensory distal latency

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 15 Change in mean sensory distal latency

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	7/20	4/18		1.58 [0.55, 4.50]
02 4 months post treatment				
Aygul 2005	10/20	5/18		1.80 [0.76, 4.27]



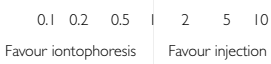
Analysis 07.16. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 16 Significant improvement digit 4 sensory latency difference median and ulnar nerves

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 16 Significant improvement digit 4 sensory latency difference median and ulnar nerves

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 weeks post treatment				
Aygul 2005	13/20	7/18		1.67 [0.86, 3.24]
02 4 Months post treatment				
Aygul 2005	12/20	6/18		1.80 [0.85, 3.79]



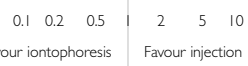
Analysis 07.17. Comparison 07 Local corticosteroid injection versus iontophoresis, Outcome 17 Significant improvement in median nerve terminal latency index

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 07 Local corticosteroid injection versus iontophoresis

Outcome: 17 Significant improvement in median nerve terminal latency index

Study	Injection n/N	Iontophoresis n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 8 Weeks post treatment				
Aygul 2005	5/20	4/18		1.13 [0.36, 3.55]
02 4 Months post treatment				
Aygul 2005	5/20	2/18		2.25 [0.50, 10.20]



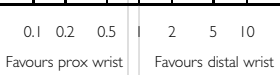
Analysis 08.01. Comparison 08 Wrist crease versus distal to wrist crease local corticosteroid injection, Outcome 01 Clinical improvement

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 08 Wrist crease versus distal to wrist crease local corticosteroid injection

Outcome: 01 Clinical improvement

Study	Distal wrist n/N	Proximal wrist n/N	Relative Risk (Fixed) 95% CI	Relative Risk (Fixed) 95% CI
01 Clinical improvement at 1 week				
Habib 2006	21/21	21/21		Not estimable
02 Clinical improvement at 3 weeks				
Habib 2006	15/21	17/21		0.88 [0.63, 1.24]
03 Clinical improvement at 6 weeks				
Habib 2006	14/21	15/21		0.93 [0.62, 1.40]
04 Clinical improvement at 12 weeks				
Habib 2006	12/21	12/21		1.00 [0.59, 1.69]

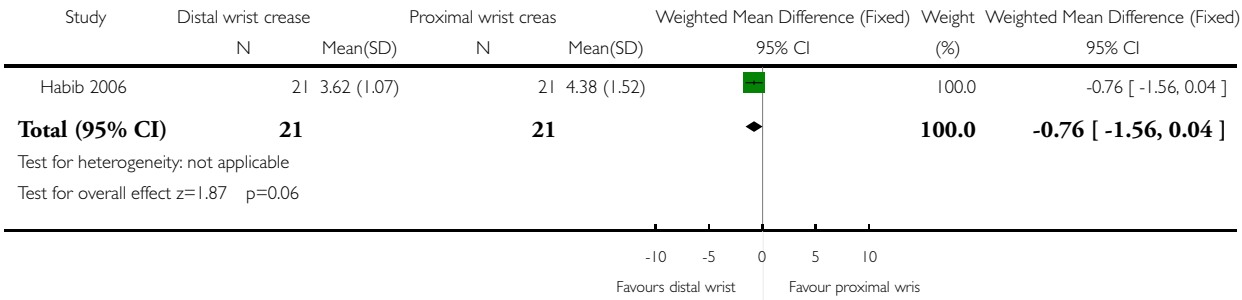


Analysis 08.02. Comparison 08 Wrist crease versus distal to wrist crease local corticosteroid injection, Outcome 02 Pain at injection site

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 08 Wrist crease versus distal to wrist crease local corticosteroid injection

Outcome: 02 Pain at injection site

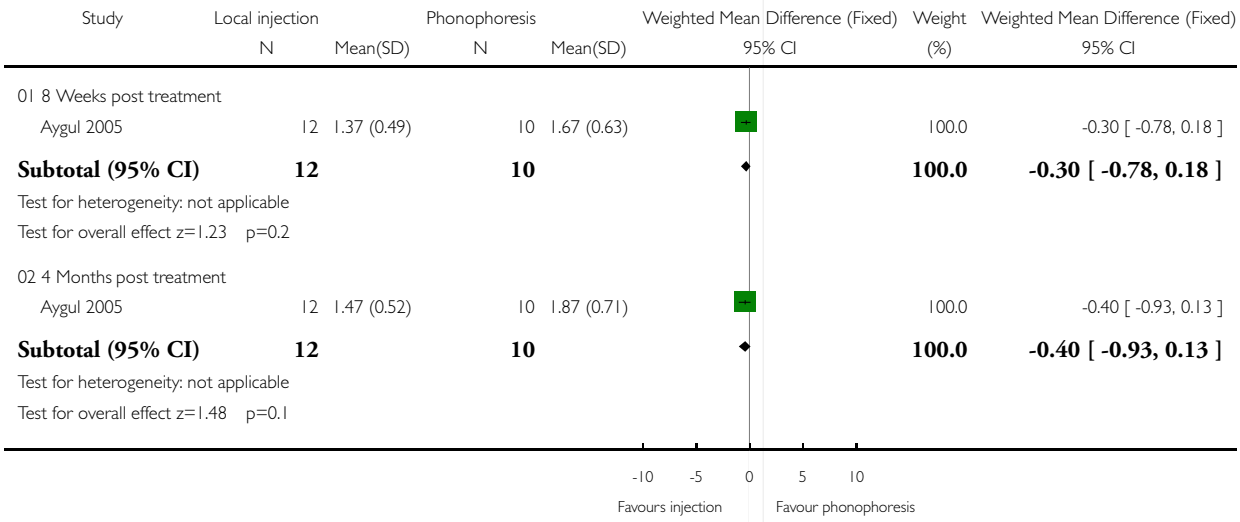


Analysis 09.01. Comparison 09 Local corticosteroid injection versus phonophoresis, Outcome 01 Symptom Severity Scale post treatment

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 09 Local corticosteroid injection versus phonophoresis

Outcome: 01 Symptom Severity Scale post treatment

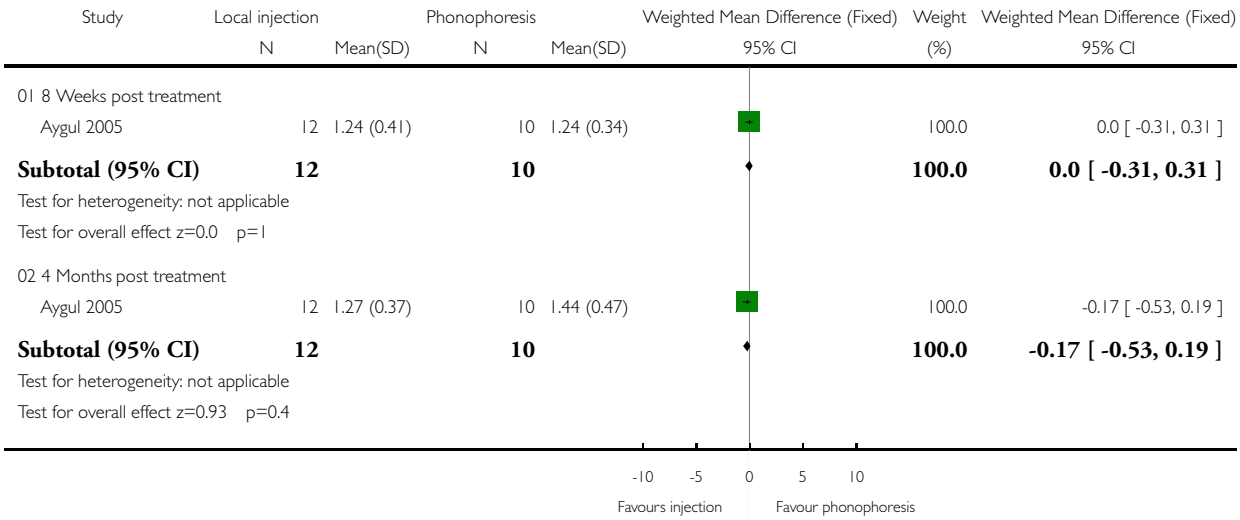


Analysis 09.02. Comparison 09 Local corticosteroid injection versus phonophoresis, Outcome 02 Functional Severity Score post treatment

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 09 Local corticosteroid injection versus phonophoresis

Outcome: 02 Functional Severity Score post treatment

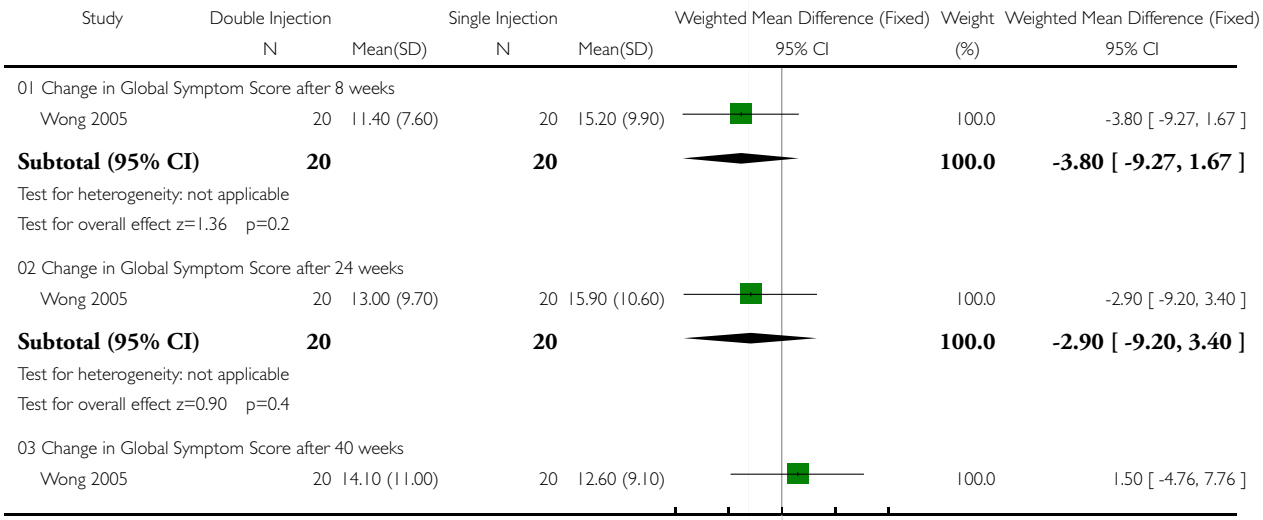


Analysis 10.01. Comparison 10 Single versus double local corticosteroid injection, Outcome 01 Global Symptom Score

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 10 Single versus double local corticosteroid injection

Outcome: 01 Global Symptom Score



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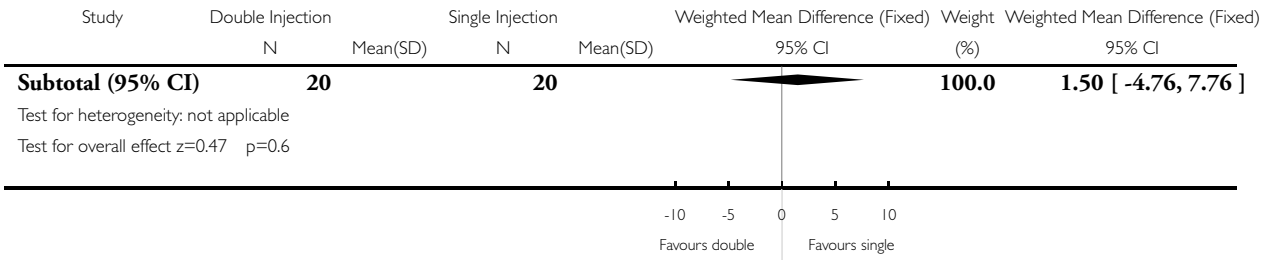
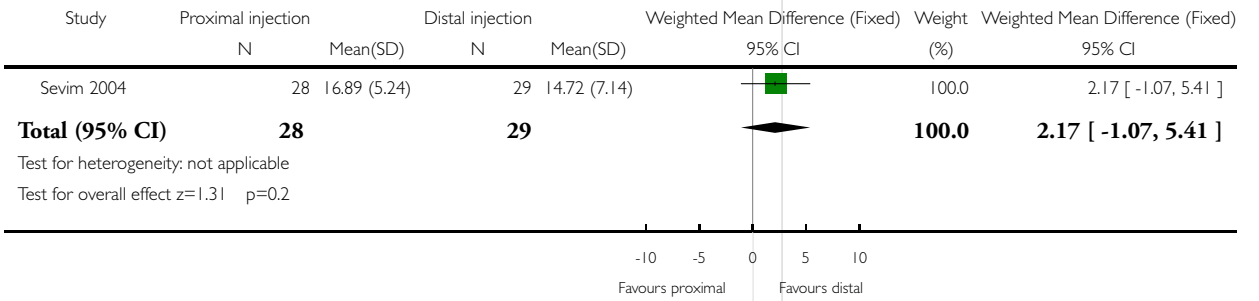


Analysis 11.01. Comparison 11 Wrist crease versus proximal to wrist crease local corticosteroid injection, Outcome 01 Neurologic Symptom Score 11 months

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 11 Wrist crease versus proximal to wrist crease local corticosteroid injection

Outcome: 01 Neurologic Symptom Score 11 months

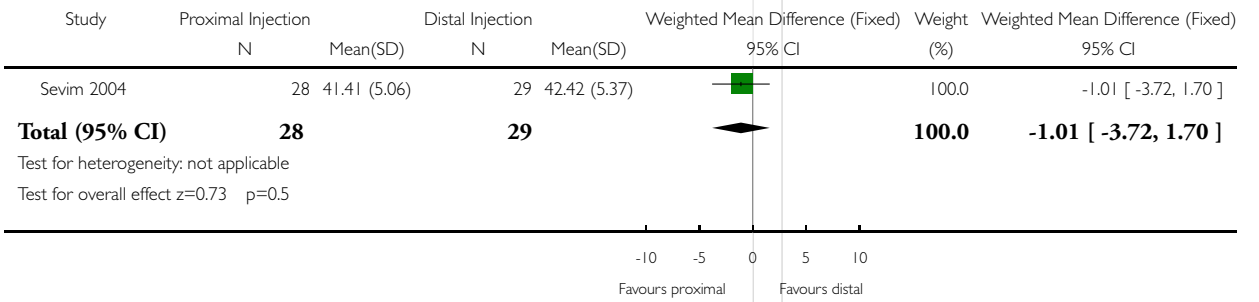


Analysis 11.02. Comparison 11 Wrist crease versus proximal to wrist crease local corticosteroid injection, Outcome 02 Mean antidromic median sensory conduction velocity digits I, II, III at 11 months

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 11 Wrist crease versus proximal to wrist crease local corticosteroid injection

Outcome: 02 Mean antidromic median sensory conduction velocity digits I, II, III at 11 months

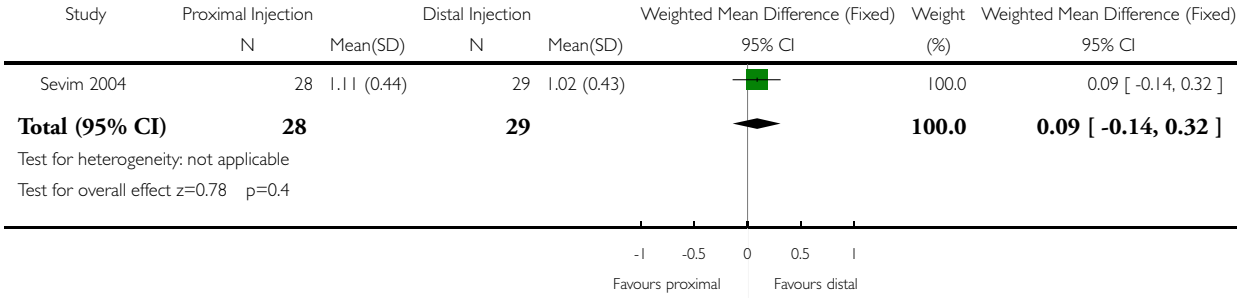


Analysis 11.03. Comparison 11 Wrist crease versus proximal to wrist crease local corticosteroid injection, Outcome 03 Median versus ulnar digit IV antidromic sensory distal latency difference at 11 months

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 11 Wrist crease versus proximal to wrist crease local corticosteroid injection

Outcome: 03 Median versus ulnar digit IV antidromic sensory distal latency difference at 11 months



Analysis 11.04. Comparison 11 Wrist crease versus proximal to wrist crease local corticosteroid injection, Outcome 04 Median second lumbrical versus ulnar interossei distal motor latency difference at 11 months

Review: Local corticosteroid injection for carpal tunnel syndrome

Comparison: 11 Wrist crease versus proximal to wrist crease local corticosteroid injection

Outcome: 04 Median second lumbrical versus ulnar interossei distal motor latency difference at 11 months