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[Intervention Review]

Intra-articular steroids and splints/rest for children with juvenile idiopathic arthritis and adults with rheumatoid arthritis

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ABSTRACT

Background

Resting or immobilizing a joint to enhance outcomes following intra-articular (IA) steroid injection is generally advocated. This systematic review aimed to determine the efficacy of IA steroid injections and the influence of post-injection rest.

Objectives

1. Compare IA steroid injections versus no treatment or placebo.
2. Determine the effects of rest following IA steroid injection in rheumatoid or juvenile idiopathic arthritis.

Search methods

The Cochrane Central Register of Controlled Trials (CENTRAL- Issue 4, 2003), Cochrane Database of Systematic Reviews (CDSR - Issue 4, 2003), Database of Abstracts of Reviews of Effectiveness (DARE - searched 8.1.04), MEDLINE (1966 to August Week 2 2004), EMBASE (1980 to August Week 2 2004), CINAHL (1982 to December Week 2 2003), Clinical Trials site of the National Institute of Health, (USA - searched 8.1.04), OTseeker (Occupational Therapy Systematic Evaluation of Evidence - searched 8.1.04) and PEDro (Physiotherapy Evidence Database - searched 8.1.04) were searched. Journals and reference lists were hand searched.

Selection criteria

Eligible were randomised controlled trials of IA steroid injections or of rest following IA steroid injections in rheumatoid or juvenile idiopathic arthritis.

Data collection and analysis

Potentially relevant references were evaluated and all data extracted by two independent reviewers.

Main results

Five trials (n=346) examining IA steroid injection in the knee joint were included. It was not possible to pool data as outcome measures, timing of follow up and the methods of data reporting differed between trials. There was inconclusive conflicting evidence from two trials that walking time was reduced. There was evidence from one moderate quality trial that pain was reduced at 1-day post-injection (0-100 VAS from 28.33 to 13.46; McGill Pain Scale from 8.89 to 3.96) but not at 1 week or 7-12 weeks post-injection. There is some evidence that IA injections improved knee flexion (by 14 degrees) and reduced knee extension lag (by 20 degrees), knee circumference (median reduction = 0.3 cm) and morning stiffness (reduced from 60 mins to 7.6 mins). One trial (n=91) examined the effects of rest following injection in

the knee. The rested group achieved significant improvement in pain, stiffness, knee circumference, and walking time when compared with the non-rested group (no point estimates provided). One trial evaluated rest following injection of the wrist (n=117). Relapse rate was higher in the rested group (rest relapse rate = 24/58, no-rest group = 14/59); but there were no differences between the rested and non-rested groups on pain, joint circumference, wrist function, grip strength or ROM.

Authors' conclusions

There is some evidence to support the use of IA steroid injections and resting a knee following injections but that wrists should not be rested following injections. The included studies involved adult participants so any conclusions can only cautiously applied to children. Further research is required to examine the use and type of rest and the differential responses of different joints following injections.

PLAIN LANGUAGE SUMMARY

Intra-articular steroids and splints/rest for arthritis in children and adults

Do intra-articular steroid injections work for treating rheumatoid arthritis and should people rest after the injections?

Seven moderate quality studies were reviewed and provide the best evidence we have today. The studies tested 346 adults with rheumatoid arthritis. They compared people who had a steroid injection, a fake injection or aspiration/washout of their knees or wrists to each other. Two studies tested whether people should rest their joints after injections.

What is rheumatoid arthritis and how might steroid injections help?

Rheumatoid arthritis is a disease in which the body's immune system attacks its own healthy tissues. The attack happens mostly in the joints of the hands and feet and causes redness, pain, swelling and heat around the joints. Intra-articular steroid injections into a joint can be used to decrease pain and swelling quickly. People may have steroid injections to delay starting steroid pills or arthritis drugs, or when drugs are not controlling pain enough. It is not clear if steroid injections work and if people should rest their joints after injections.

What did the studies show?

One of two studies show that people who had steroid injections had less pain the first day than people who had fake injections.

Pain decreased by about 15 points on a 0-100 scale with a steroid injection and 7 points with a fake injection.

The change in pain, however, was the same after 1 or 7 to 12 weeks with or without steroid injections.

Studies show that people who had steroid injections could bend and straighten their leg better/farther and had less swelling around their knee than people with fake injections. Morning stiffness also did not last as long with steroid injections. But one study shows that people could walk faster with steroid injections while another study shows they could not.

People had less pain, stiffness, swelling, and could walk faster if they rested their knees after steroid injections to their knees. But after steroid injections to their wrists, people felt the same whether they rested their wrists or not - but more had a relapse when they rested.

How safe are steroid injections?

No side effects due to injections were reported.

What is the bottom line?

The level of quality of the evidence is 'silver'. Intra-articular steroid injections can improve pain, movement, stiffness and swelling and are safe in adults with rheumatoid arthritis. There is no evidence to say whether this is true for children.

Knees should be rested after a steroid injection, but wrists should not.

BACKGROUND

Rheumatoid arthritis is a chronic disease characterised by swelling, inflammation or limitation of movement in at least one joint, with pain, heat and/or tenderness in the affected joints. Loss of function may accompany arthritis. Juvenile idiopathic arthritis (JIA) is a chronic arthritis of unknown origin that begins before age 16 and persists at least six weeks to three months (Cleary 2003).

Intra-articular (IA) steroid injections are accepted practice in the clinical management of both adults and children with arthritis (Dent 1998). IA injections were the second most common therapy (after non-steroidal anti-inflammatory drugs) used by Canadian and US pediatric rheumatologists in managing pauci-articular (oligoarthritis) JIA (Cron 1999). IA injections are used to provide local, immediate anti-inflammatory effects to the injected joint (Cleary 2003). The joint capsule is entered with a needle and the corticosteroid is injected. Fluid may be aspirated out of the joint prior to injection (arthrocentesis) as there is some evidence that this procedure reduces the risk of relapse following injection (Weitof 2000). IA steroid injections are used as first line agents when, for example, only one or two joints are affected by arthritis and/or to prevent or delay the need for oral steroids or other systemic drugs such as methotrexate (Cleary 2003, Dent 1998, See 1998). IA steroid injections can also provide relief whilst awaiting the onset of disease modifying drugs. In addition, IA steroid injections may be used as second line therapy to manage joints with a poor response to non-steroidal anti-inflammatory medications (Cleary 2003).

Although IA steroid injections are widely used in the clinical management of children and adults with arthritis, the evidence for the efficacy of IA steroid injections has not yet been systematically reviewed. There are several retrospective audits and pre-post design studies examining the outcome of IA steroid injections (e.g., Allen 1986, Hertzberger-ten Cate, Hollander 1951, Huppertz 1995, Lepore 2002, McCarty 1972, McCarty 1995, Neidel 2002, Padeh 1998). These studies report positive outcomes of injections with few, if any, adverse events. For instance Allen 1986 injected 49 knees in children and reported that 50% of children had maintained a good response at one year. Huppertz 1995 injected various joints of 21 children and reported that all the joints improved at seven weeks on MRI. Padeh 1998 injected a mix of joints in 71 children and reported that 82% of joints remained in remission at six months. Similarly Hertzberger-ten Cate reported 70% remission at six months in 21 injected knees and Neidel 2002 reported a 58% remission rate at two years from 67 injected hips.

Resting or immobilizing a joint to enhance outcomes following IA steroid injection is advocated by a number of authors. The rationale for resting a joint includes:

1. Reducing the amount of steroid diffusion out of the joint (Chakravarty 1994, McCarty 1995), thus allowing time for repair of inflamed tissue (McKenzie1997, Chatham 1989, McCarty 1995) and minimising any effects of the steroid in other parts of the body (systemic effects) (Neustadt 1985).
2. Minimising the leakage of steroid back through the track the needle makes as it enters the joint (needle track) (McCarty 1995).
3. Preventing people who may receive immediate pain relief from the injections from over-using joints (Chakravarty 1994).

Rest may be achieved through bedrest, reduced activity levels or splinting. The nature of the rest and the period for which

it is imposed varies greatly amongst those recommending it. A survey of British rheumatologists (Haslock 1995) reported that "most" respondents advised rest or reduced use of injected weight bearing joints for periods of between 12 to 24 hours post-injection and that admission for bedrest was practiced by nearly 14% of respondents. Bedrest regimens include 24 hours (Chakravarty 1994) or 48 hours (Chatham 1989) of bed rest in hospital, and three days of bedrest followed by three weeks of reduced activity (Neustadt 1985). Avoiding activity including weight bearing for 24 hours has been recommended (Honkanen 1993, Padeh 1998), as has full time splint use for 48 to 72 hours following injections (McKenzie1997). A longer three-week period of either splinting to immobilise wrists and fingers or restricted use for other upper limb joints and six weeks of restricted use for the lower limb has also been suggested (McCarty 1972, McCarty 1995). In contrast some researchers advise IA steroid injection recipients to pursue their usual activities following injections (Hollander 1951) and others make no mention of rest or splints as part of the IA steroid injection management (Allen 1986, Bird 1979, Hertzberger-ten Cate, Huppertz 1995).

There are, therefore, few controlled studies of intra-articular injections and of resting or splinting joints following injections. This systematic review of RCTs is being undertaken to determine whether intra-articular steroid injections result in better outcomes than no treatment or placebo and whether splints/rest influence outcome. As the impetus for this review arose in a children's hospital we proposed to review the efficacy of IA steroid injections and resting post-injections in children with arthritis. A preliminary search of the literature, however, revealed no RCTs of children with arthritis so this systematic review was broadened to include RCTs of adults with rheumatoid arthritis with the intention of generalising, where appropriate, to children.

OBJECTIVES

1. To assess the effectiveness and safety of intra-articular steroid injections compared to no treatment or placebo in people with rheumatoid or JIA. [Note that placebo includes injection of saline, joint washout or aspiration. Joint washout involves aspirating synovial fluid, then injecting saline and aspirating it out of the joints one or more times to remove intra-articular debris (Srinivasan 1987)]
2. To assess whether resting a joint, including using splints, immediately following intra-articular steroid injections in people with rheumatoid or JIA contributes to an improved outcome compared to IA steroid injection without rest.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials were eligible for inclusion.

Types of participants

All studies of subjects with arthritis (rheumatoid and juvenile idiopathic) were eligible for inclusion. Studies of osteoarthritis were excluded as this population is not relevant to children with JIA.

Types of interventions

Studies were eligible for inclusion if they compared:

I Intra-articular steroid injections with no treatment or a placebo. A placebo includes joint washout, aspiration or injection of saline or vehicle.

II Either rest or splints with no rest/splint following IA steroid injection management.

Types of outcome measures

Patient centred disability measures were considered where appropriate as suggested by [Giannini 1997](#) and [Boers 1994](#) as were the OMERACT 1993 measures as follows:

Effectiveness:

- Functional status (e.g. self care ability, walking ability)
- Pain
- Range of motion
- Joint circumference
- No of tender joints per patient
- Number of swollen joints per patient
- Time until exacerbation of symptoms such as joint pain, swelling, functional limitation
- Quality of life
- Parent/patient global assessment
- Physician global assessment
- Acute phase reactants

Safety:

- Adverse events related to splinting
- Adverse events related to steroid injections
- Numbers of withdrawals due to lack of efficacy and side effects.

Search methods for identification of studies

The Cochrane Database of Systematic Reviews (CDSR - Issue 4, 2003) and the Database of Abstracts of Reviews of Effectiveness (DARE - searched 8.1.04) were searched to identify any relevant systematic reviews.

The Clinical Trials site of the National Institute of Health, (USA - searched 8.1.04), PEDro (Physiotherapy Evidence Database - searched 8.1.04), OTseeker (Occupational Therapy Systematic Evaluation of Evidence - searched 8.1.04) and the Cochrane Central Register of Controlled Trials (CENTRAL- Issue 4, 2003) were searched for trials.

MEDLINE (1966 to August Week 2 2004), EMBASE (1980 to August Week 2 2004) and CINAHL (1982 to December Week 2 2003) were also searched for clinical trials. The Topic search strategy is shown in [Appendix 1](#) and is based on the Cochrane Musculoskeletal Group strategy. This strategy was used to search MEDLINE, together with a standard randomised controlled trial filter, and adapted appropriately for other databases.

Non-English language articles were eligible for selection to reduce the risk of publication bias.

The reference lists of relevant studies were searched for further identification of published work, conference presentations and personal communication.

The following rheumatology journals were hand searched for studies and conference proceedings

- Arthritis and Rheumatism (searched to Volume 48(12) 2003)
- Journal of Rheumatology (searched to Volume 30(8) 2003)
- Rheumatology (formerly British Journal of Rheumatology; searched to 42(12) 2003)
- Arthritis Care and Research (searched to 49(5) 2003)

Data collection and analysis

Selection of studies

This review was preceded by a peer reviewed published a priori protocol.

The above search strategy identified a set of potentially relevant references (title/abstracts). Full articles were obtained where a judgement about the suitability of inclusion could not be made from the title/abstract or when consensus could not be reached. Potentially suitable references were then assessed independently by two reviewers (MW, DG) according to the selection criteria to determine which ones were eligible for inclusion. Differences were resolved by consensus. A standard data extraction form was devised and piloted. Data were extracted independently by the two reviewers (MW, DG) who then met to compare the data. Any differences between reviewers were resolved by discussion and consensus. If data were missing or further information was required, reasonable attempts were made to contact the authors to request required information.

In addition to extracting data the reviewers independently allocated each included trial into one of three quality categories, based on those described in the Cochrane Reviewers' handbook version 4.0 (section 6.7.1, page 39):

- Category A: Low risk of bias - plausible bias unlikely to seriously alter the results - All the criteria met
- Category B: Moderate risk of bias - plausible bias that raises some doubt about the results - One or more criteria met
- Category C: High risk of bias - plausible bias that seriously weakens confidence in the results - One or more criteria not met

The criteria for assessment were: random allocation, allocation concealment, blinding, accounting for withdrawals and dropout rate

Differences in the reviewers allocation of studies into quality categories were resolved by consensus.

Data Analysis:

Where possible weighted mean differences and 95% confidence intervals were calculated for continuous outcomes and dichotomous outcomes were analyzed using relative risks and 95% confidence intervals. Meta-analysis was planned if similar outcomes were available in clinically similar populations (e.g. diagnostic groups, joints injected) and measured at similar time points post-injections. Data for different joints were analysed separately. Significance for statistical heterogeneity was set at 0.10, using a chi square analysis.

Following review of all identified studies, however, there were no included studies where data for common outcomes measures collected at similar points in time and for the same joints (e.g. knees or wrists) could be pooled in a meta-analysis. In addition, a sensitivity analysis was planned to determine whether trials allocated to Category C should be included in the data analysis but

this was not possible as no data from any of the studies could be pooled.

As studies reported data collected at different times post-injection it was decided to present data in time intervals; these were 1 day, 1 week, 2 to 6 weeks, 7 to 11 weeks, and 12 to 24 weeks. These time intervals were selected post-hoc and were intended to represent clinically meaningful time frames.

Grading of evidence

We used the grading system described in the 2004 book Evidence-based Rheumatology (Tugwell 2004) and recommended by the Musculoskeletal Group:

Platinum: A published systematic review that has at least two individual controlled trials each satisfying the following:

- Sample sizes of at least 50 per group - if these do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
- Blinding of patients and assessors for outcomes.
- Handling of withdrawals >80% follow up (imputations based on methods such as Last Observation Carried Forward (LOCF) are acceptable).
- Concealment of treatment allocation.

Gold: At least one randomised clinical trial meeting all of the following criteria for the major outcome(s) as reported:

- Sample sizes of at least 50 per group - if these do not find a statistically significant difference, they are adequately powered for a 20% relative difference in the relevant outcome.
- Blinding of patients and assessors for outcomes.
- Handling of withdrawals > 80% follow up (imputations based on methods such as LOCF are acceptable).
- Concealment of treatment allocation.

Silver: A systematic review or randomised trial that does not meet the above criteria. Silver ranking would also include evidence from at least one study of non-randomised cohorts that did and did not receive the therapy, or evidence from at least one high quality case-control study. A randomised trial with a 'head-to-head' comparison of agents would be considered silver level ranking unless a reference were provided to a comparison of one of the agents to placebo showing at least a 20% relative difference.

Bronze: The bronze ranking is given to evidence if at least one high quality case series without controls (including simple before/after studies in which patients act as their own control) or if the conclusion is derived from expert opinion based on clinical experience without reference to any of the foregoing (for example, argument from physiology, bench research or first principles).

RESULTS

Description of studies

Initially, 15 studies were identified from the literature search. Eight of these studies were excluded - see Table of Excluded Studies. Following is a brief description of the seven remaining studies (see Table of Included Studies).

Chandler 1958 completed a double-blind crossover trial of 24 adults with rheumatoid arthritis. Thirty-seven knees from these participants were injected with hydrocortisone acetate, hydrocortisone tertiary butyl acetate or placebo. Outcomes

measured included walking time, ROM and pain, measured at fortnightly intervals during the follow up period. Significance levels for the differences between groups, but not point estimates or variances, were reported in the paper. As the authors have not been able to be contacted (see Table of Included Studies) there is no information which can be used in a meta-analysis. The results of this study, therefore, will be discussed descriptively in the Results section.

Grewin 1988 and colleagues studied 73 participants with arthritis of the knee who were randomised to receive 80 mg methylprednisolone acetate, 20 mg or 40 mg triamcinolone hexacetone or placebo. The outcome measures included joint index and duration of efficacy. **Grewin 1988** published the work in abstract form and the authors have not been able to be contacted for details of the study or results (see Table of Included Studies). Thus, only mean values (no variance) for duration of efficacy and statistical difference between groups for joint index are available for inclusion in a descriptive discussion. Methodological quality is unable to be assessed as insufficient information is provided in the abstract.

Srinivasan 1987 randomly allocated 60 participants with active synovitis of the knee into three groups: Group 1 - aspiration and triamcinolone; Group 2 - aspiration and washout; Group 3 - aspiration, triamcinolone and washout. The groups appropriate for comparison are Groups 2 and 3. Median and range data, which are inappropriate to include in a meta-analysis, were reported for the outcomes of pain, morning stiffness, joint circumference, walking time and ROM. This paper has been designated as having a moderate risk of bias and the data will be discussed descriptively.

Stein 1999 carried out an RCT where 52 participants with either rheumatoid arthritis (RA) (n=24) or osteoarthritis (OA) (n=28) were randomly allocated to receive intra-articular morphine, dexamethasone or placebo injection to the knee. The study reported no significant difference between the RA and OA groups on the outcomes therefore these data were not reported separately for each patient group in the published paper. Outcomes were pain VAS and the McGill Pain Questionnaire. Data (means and standard deviations) were reported hourly for six hours and daily for six days. Only the data from hour six (Day 1) and day six (one week) are used in this review as these were the data points closer to the time frames selected. This paper is designated as having a moderate risk of bias.

van Vliet 1987 and colleagues randomised 137 participants with rheumatoid arthritis to receive 10 mg, 20 mg or 40 mg Rimexolone (Vexol) or a placebo injection to the knee. Follow up was at one week, one, two and three months and the outcomes included knee circumference and knee flexion. A number of other outcomes were measured but they were developed for the study and do not have established psychometric properties (see Table of Included Studies). Means and standard deviations for these outcomes were available however, these data could not be pooled with data from any other study. This study was designated as having a moderate risk of bias due to a large drop-out rate of 40% by the three month follow up (drop out rate at one week = 5%, one month = 12%, two months = 32%).

Chakravarty 1994 was one of only two included studies to investigate the effects of rest following IA injections (triamcinolone hexacetide). Ninety-four participants with arthritis in the knee were randomised to receive an injection only or injection plus 24 hours

of strict, non-weight bearing rest (bedrest). The outcomes were pain, stiffness, knee circumference and walking time measured at baseline, 3, 6, 12 and 24 weeks. The median and interquartile range of the area under the response curve for each outcome measure were reported, therefore, these data could not be used in a meta-analysis. This paper is designated as having a moderate risk of bias.

Weitoft 2003 evaluated the effects of 48 hours of rest using an elastic wrist orthoses following IA injections in 117 participants with RA of the wrist. The primary outcome was relapse of synovitis; the secondary outcomes were pain, wrist extension, joint circumference, wrist function and grip strength. All data are available for meta-analysis although with no other studies of wrists, there is no capacity to pool data. This study is designated as having a moderate risk of bias.

In summary, of the seven included studies, five compared IA steroids to placebo. Chandler 1958 and Grewin 1988 did not include data which could be entered into a meta-analysis and Srinivasan 1987 reported median and range data which could not be included in a meta-analysis. Stein 1999 and van Vliet 1987 provided detailed results which are useful for quantitative analysis. Chakravarty 1994 was the only included study to compare rested and non-rested knees following injections but this paper did not report data which could be used in a meta-analysis. Weitoft 2003's study of rest following injection provided data for analysis.

Risk of bias in included studies

The included studies were categorised into one of three quality categories, based on those described in the Cochrane Reviewers' handbook version 4.0 (section 6.7.1, page 39).

They were as follows:

I: IA steroid versus placebo

Chandler 1958: Moderate risk of bias - random allocation, unclear allocation concealment, adequate blinding of participants and observers, withdrawals accounted for, drop out rate 25%

Grewin 1988: Unable to categorise as insufficient information was available in the abstract located.

Srinivasan 1987: Moderate risk of bias - random allocation, unclear allocation concealment, observer blinding, no information regarding existence of dropouts

Stein 1999: Moderate risk of bias - random allocation, unclear allocation concealment, participants and observers blinded, reasons for withdrawal noted and 15% drop out rate.

van Vliet 1987: Moderate risk of bias - random allocation, unclear allocation concealment, participants and observers blinded. The drop out rate was high. For example the drop out rate for the 10 mg, 20 mg, 40 mg and placebo groups respectively at 3 months were 34%, 31%, 33% and 59%. The total drop out rate was 40%. The reasons for drop out were predominantly no, poor or negative effect.

II: Rest versus no rest

Chakravarty 1994: Moderate risk of bias - random allocation, unclear allocation concealment, blinding of observers, accounted for withdrawals, low drop out rate.

Weitoft 2003: Moderate risk of bias - random allocation, unclear allocation concealment, blinding of observers, accounted for withdrawals, low drop out rate.

Effects of interventions

I: EFFICACY OF IA INJECTION VERSUS PLACEBO

Walking time

One of the two studies measuring walking time reported no significant difference.

- Srinivasan 1987 (n=60; no Metaview data) reported no significant difference between groups in change in walking time between groups. The time to walk 50 yards was reduced by 6 seconds in the placebo group and 3.5 seconds in the steroid group at three months.
- Chandler 1958 (n=24; no Metaview data) reported a significant reduction in walking time in the IA injection steroid group compared to the placebo groups at two weeks ($p<.01$) and four weeks ($p<.05$), the actual values were not reported.

Pain

One of two studies reported a significant reduction in pain at rest at one day post-injection. There was no treatment effect at one week (1 study) or 7-12 weeks (1 study).

- Srinivasan 1987 (n=60; no Metaview data) reported no statistical difference in pain between placebo and steroid groups using a VAS at three months.
- Stein 1999 (n=52; see Metaview graph) found a significant reduction in pain (VAS at rest and McGill Pain Scale) in the IA steroid group compared to the placebo group at day one but not one week. Pain during activity (VAS) was not significantly reduced at either time point.

Knee flexion

- Srinivasan 1987 (n=60; no Metaview data) reported that, at three months, the steroid group achieved significantly more knee flexion following injection compared to the placebo group (steroid group increased 14 degrees and the placebo group increased one degree, ($p<.01$)).
- van Vliet 1987 (n=137; see Metaview graph). When the three doses (10, 20, and 40 mg) were compared to the placebo, the only significant improvement compared to placebo was in the 40 mg dose at 28 days.
- Chandler 1958 (n=24; no Metaview data) reported significantly increased knee flexion at two ($p<.05$), four ($p<.05$), six ($p<.05$) and eight weeks ($p<.05$) in the steroid group compared to the placebo group.
- In summary: there is some evidence that IA injections improve knee flexion. Van Vliet found no effect except at the higher dose at 2-6 weeks and Srinivasan 1987 and Chandler 1958 provide evidence of a moderate improvement up to 7-12 weeks although there was no effect in van Vliet 1987 study during the same time period.

Extension lag

- Srinivasan 1987 (n=60; no Metaview data) reported a significant improvement in extension lag in the IA steroid group at three months (from 20 to 0 degrees, $p<.02$); compared to the placebo group (from 3.5 to 5 degrees). However, the differences in baseline extension lag between groups may have biased the results in favour of the steroid group.

- [Chandler 1958](#) (n=24; no Metaview data) reported a significant improvement in extension lag in the IA steroid group compared to the placebo groups at two (p<.02), four (p<.05), six (p<.01) and eight weeks (p<.05).
- In summary: there is some evidence supporting the effects of IA injections in reducing extension lag at 2-6 weeks and 7-12 weeks.

Knee circumference

- [Srinivasan 1987](#) (n=60; no Metaview data) reported no change in the median knee circumference at three months in the placebo group and a reduction of 0.3 cm in the steroid group. Although this difference in groups was statistically different (p<.002), the clinical significance of this difference is questionable.
- [van Vliet 1987](#) (n=137; see Metaview graph) found a treatment effect from IA steroid injections only for the 40 mg (highest) dose at one week and 28 days.
- In summary: there is some evidence that knee circumference is reduced (van Vliet) at one week and at 2-6 weeks by the higher dose. There is inconclusive evidence at 7-12 weeks (difference of 0.3 cm; Srinivasan) regarding knee circumference and no treatment effect observed at 13-24 weeks (van Vliet).

Morning stiffness

- [Srinivasan 1987](#) (n=60; no Metaview data) reported a significant decrease in morning stiffness in the steroid group compared to the placebo group at three months (placebo median at baseline = 90 minutes, three months = 60 minutes; steroid median at baseline = 60 minutes, three months = 7.6 minutes, p<.04). This also appears clinically significant.
- In summary: there is moderate evidence from one study that morning stiffness is reduced at 7-12 weeks using a patient rating of duration of morning stiffness.

Joint index

- [Grewin 1988](#) (n=73; no Metaview data) did not provide data or statistical test results for this outcome but did report significantly better response to IA injection of steroid compared to placebo in the published abstract.

Duration of efficacy

- [Grewin 1988](#) (n=73; no Metaview data) reported that duration of efficacy in the three steroid groups was 11.4, 20.5 and 22.3 weeks compared with one week in the placebo group. No further information was reported in this abstract.

Adverse events

The only studies that reported adverse events were:

- van Vliet - reported dose-related serum rimexolone levels in the rimexolone groups. Data were not statistically analysed but there appears no difference between treatment and placebo groups in the incidence of post injection flare-up, local pain, systemic effects or intercurrent symptoms (which included rash, perspiration, shivering, influenza and gastrointestinal symptoms).
- [Chandler 1958](#) - this study reported transient exacerbation of arthritis which resolved by day 3 following injections in 2 participants from a treatment group; and 3 participants who developed DVT (2 from the treatment, 1 from the placebo group).

II: REST VERSUS NO REST

Knees:

[Chakravarty 1994](#) (n=91; no Metaview data) was the only study to investigate rest following IA injections. The information in [Table 1](#) refers to median summary measures of response (area under the curve, total follow up time of three months) for each variable (pain, stiffness, knee circumference, walking time) and the p-value. The rest group experienced significantly more improvement than the non-rest group on all the variables. No other data were provided in this paper.

Wrists:

[Weitoft 2003](#) (n=117; see Metaview graphs). The primary outcome measure was relapse of wrist synovitis. [Weitoft 2003](#) reported no significant difference between groups in the proportion of relapse (rest relapse rate = 24/58, no-rest = 14/59; Chi sq: p=0.056). This data entered into MetaView however indicated that the relapse rate was greater in the rest group (OR=2.27; 95% CI 1.02 to 5.03). There was no difference between groups for any of the secondary outcomes (pain, joint circumference, wrist function, ROM and grip strength).

DISCUSSION

This systematic review and meta-analysis is a synthesis of RCTs of IA steroid injections versus placebo or no treatment, and RCTs of resting a joint following injections.

Five RCTs which addressed the effectiveness of IA injections over placebo were identified, all of which studied adults with arthritis. Overall, there is some evidence that injections improve pain (at one day), knee flexion and extension lag (up to 7 to 12 weeks), knee circumference (up to 2 to 6 weeks), morning stiffness (up to 7 to 12 weeks) and duration of efficacy (11.4 to 22.3 weeks in the steroid-treated groups vs 1 week in the placebo control group). The evidence in support of the effectiveness of IA on walking time is inconclusive. There is also some suggestion that the effectiveness of IA steroid may be dose-related. There were no reported adverse events related to the injections in recent studies. In summary, there is weak RCT evidence in support of IA steroid injections in managing adults with rheumatoid arthritis. There is no evidence of harm so it is appropriate that IA steroid injections continue to be used and to be properly evaluated. It is important to note that all the included studies evaluated the outcomes of injected knees. The impact of IA steroid injections on other joints can only be extrapolated and requires investigation.

Resting a joint following injections is an imposition for the patient and, depending on the method used (e.g. hospitalisation, splints), the health system. The efficacy of rest needs to be evaluated in order for rest to be used confidently as part of IA steroid management in arthritis. One RCT ([Chakravarty 1994](#)) investigating rest versus no rest following IA injection in the knee was located. Results for pain, stiffness, knee circumference and walking time indicated that rest is effective in enhancing the outcomes of IA steroid injections. Conversely, a second RCT ([Weitoft 2003](#)) reported no difference in the relapse rate between a rested and non-rested group following injections to the wrist. Further analysis of the relapse rate in Metaview suggests that the relapse rate of wrist synovitis was actually greater in the rest group. There is some evidence, therefore, to support the use of rest following IA injections in the knee, but further research is required. Resting the

wrist joint ,however, following injection appears unnecessary and may even cause harm.

The reason for the discrepancy in results for resting knees versus wrists following IA injections is not clear. Both studies are designated as having moderate risk of bias and use reliable outcome measures, so methodological quality is not likely to be responsible for the differences. Although [Chakravarty 1994](#) does not report sufficient data to allow analysis in Metaview, the results indicate that rest enhances outcomes for knees following IA injections. [Weitoft 2003](#) proposes the following reasons why the results of his trial differ from those of [Chakravarty 1994](#): i) absorption of corticosteroid may be increased by weightbearing and, as a non-weight-bearing joint, the wrist does not require resting; ii) the smaller area of inflamed synovium in the wrist means that less corticosteroid is absorbed and immobilisation may be of minor importance; or iii) wrist movement may be necessary to spread the corticosteroid around the wrist joint complex and tendon sheaths so rest may inhibit this process. A further possibility is that the elastic wrist orthosis used by [Weitoft 2003](#) does not immobilise the wrist sufficiently to be effective.

There are many questions which remain unanswered regarding rest and IA steroid injections. The [Chakravarty 1994](#) study described the effectiveness of 24 hours of inpatient bedrest following injections, [Weitoft 2003](#) used 48 hours of elastic wrist orthosis. As well as replicating these studies, further research is required to evaluate the effects of other means of rest (such as rigid splints and casts) and of rest on other joints such as hips, ankles and finger joints. In addition, more work is needed to determine the length of rest that is most effective in enhancing the outcomes of IA steroid injections. Finally, the issue of IA injections and rest in children with JIA has not been studied in clinical trials. Any conclusion drawn from the adult literature must be carefully considered before being extrapolated to children with JIA.

In conclusion, there is:

"silver" level evidence for the efficacy of IA injections in managing rheumatoid arthritis

"silver" level evidence that resting knee joints after IA injections is beneficial and

"silver" level evidence that wrists should not be rested after IA injections.

AUTHORS' CONCLUSIONS

Implications for practice

IA steroid injections are commonly accepted practice in the management of rheumatoid and JIA ([Haslock 1995](#)). This systematic review of RCTs in the area provides some evidence for IA steroid injections and for resting knees following injections in adults. This review concludes that resting wrist joints may not be required and may be harmful. Further research is required to confirm the place of IA injections in the management of arthritis and the use of rest following injections in adults and especially in children.

Implications for research

The evidence surrounding the efficacy of IA injections and the impact of rest following injections is drawn from a small numbers of studies with small numbers of participants. The studies of IA injection efficacy lacked uniformity of outcome measures and follow up periods which limited the ability to pool data in a meta-analysis. Large and rigorous RCT's are required to further investigate the role of IA steroid injections in effecting meaningful change for people with rheumatoid arthritis and in children with JIA. The need for rest following injections, as well as the optimum type and duration of rest, also requires exploration.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Chakravarty 1994

Methods	RCT of bedrest versus no bedrest following steroid injection. Baseline: The rest group had significantly more stiffness and smaller knee circumference (probably not clinically significant). No other differences.
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Chakravarty 1994 (Continued)

Drop outs: at 12 weeks 3% (1 in rest group, 2 in non-rest group did not want to continue), at 24 weeks 20.2% (16 required a change in treatment, 4 from the rest group, 12 from the non-rest group).

Participants	91 consecutive patients with inflammatory arthritis in 1 knee attending routine rheumatology outpatient clinic in UK. Exclusions: multiple joint inflammation, non inflammatory synovitis, chondro calcinosis, change of treatment or IA/systemic steroids in previous 3 months.
Interventions	Rest consisted of 24 hours of strict non-weightbearing bed rest in hospital vs no rest in people injected with Triamcinolone hexacetonide 40mg plus 2 ml 2% lignocaine (aseptic technique). Aspirated to near dryness when effusion present.
Outcomes	Included outcomes: Pain (10cm VAS), walking time for 50 feet (secs), knee circumference (cm), stiffness (10cm VAS). Measures at baseline, 3, 6, 12 and 24 weeks. No adverse events.
Notes	Median response curves over the follow up times and between groups were reported. The author was not able to provide mean and standard deviation data for the outcomes at each time point for inclusion in Metaview. 16 participants dropped out between 12 weeks and 24 weeks and their data were assumed to have returned to baseline for intention-to-treat analysis.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Chandler 1958

Methods	Double blind crossover trial of steroid and placebo. Blinding: participants and observers. No baseline data provided. Drop out: 25%, Reported to be distributed evenly between groups, but rates not reported for each group. The reasons given were that 4 required admission due to deterioration in arthritis, 1 developed an unrelated disease and 1 participant defaulted without reason given.
Participants	24 outpatients with 37 knees with active inflammatory changes, UK. Exclusions: systemic or IA steroids in previous 2 months.
Interventions	Hydrocortisone acetate vs hydrocortisone tertiary butyl acetate (25mg/ml vehicle) vs placebo (1ml vehicle). Each drug was administered fortnightly for 8 weeks with an 8 week follow up. This was repeated for the next randomly assigned drug until each participant received each intervention.
Outcomes	Included outcomes: extension lag, walking time over 75 yards, ROM (although it is not specified it is assumed that ROM means knee flexion). Excluded outcomes: Pain (scale of 0 to 4 lacks reliability/validity), tenderness (lacks reliability/validity). Measures at baseline and fortnightly during injection and rest periods, but data are reported for 2, 4, 6 and 8 weeks during the follow up period. Adverse events: 2 participants had local and transient exacerbation of arthritis for 1 and 3 days (group not specified), 3 participants had DVT - 2 from a hydrocortisone group, 1 from placebo.
Notes	Point estimates and variance were not reported in this paper so data are unable to be pooled. Extensive efforts were made to contact the principal and co-authors but with no success due to the age of the publication.

Risk of bias

Chandler 1958 (Continued)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Grewin 1988

Methods	Double blind controlled study of IA steroids vs placebo. Blinding: participants and observers blinded. Dropouts: unclear, possibly 3% (n=2).
Participants	73 participants with active arthritis of the knee. Sweden.
Interventions	Methyl prednisolone acetate, triamcinolone hexacetonide 20mg and 40mg and placebo.
Outcomes	Included outcomes: Joint index (not specified), duration of efficacy. Excluded outcomes: overall participant judgement of efficacy and duration of the treatment. Measures at baseline and 'regularly' for 28 weeks or until improvement of joint index compared with baseline was <25%.
Notes	Insufficient data obtained from an abstract. Extensive efforts were made to contact the principal and co-authors, we believe we obtained email and postal addresses but no response has been received from them.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Srinivasan 1987

Methods	RCT comparing joint washout and IA steroid injection separately and in combination in knees. Blinding: participants - not stated; observers - yes. Baseline differences, Group 3 appears to have greater extension lag - no statistical analysis. No information about existence of drop outs.
Participants	60 adult patients with RA of the knees involving active synovitis and effusion. Age: 24 - 81 yrs, mean disease duration = 10.3yrs, 12 males, 48 females. Exclusions: Grade 4 radiological joint disease (advanced), previous surgery to joint under study, history of septic arthritis, IA steroid injection within previous 3 months. Setting: OP clinic in unstated setting.
Interventions	IA injection of 20mg triamcinolone vs 2 joint washouts using 20ml normal saline vs IA injection of 20mg triamcinolone plus 2 joint washouts using 20ml normal saline. Relevant comparisons are between the latter two groups.
Outcomes	Outcomes included: Pain (10cm VAS), joint circumference (cm at mid knee), walking time over 50 yards (seconds), joint movement (degrees of flexion, extension lag) morning stiffness (mins). Measures at baseline, 4 weeks (not reported) and 12 weeks.
Notes	Median and range data provided. Baseline differences between groups for knee extension lag are large and may have resulted in biased results.

Srinivasan 1987 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Stein 1999

Methods	RCT, double blind of IA steroid vs placebo. Blinding: participants and observers blinded. Baseline: no analysis done. Dropouts: 14% (n=5), all in placebo group: 2 experienced an increase in pain and reason is not clear in the remaining 3.
Participants	52 participants, 24 with RA, 28 with OA. Separate data were not available for RA and OA groups on any variables so analysis is presented for whole group. 67% women, mean age in "the 60's". Exclusions: bacterial synovitis, recent knee joint trauma.
Interventions	4mg dexamethasone in 3ml saline vs placebo 3ml saline vs IA morphine (not included in this review). Injections following aspiration.
Outcomes	Included outcomes: Pain (100mm VAS) at rest and during activity, McGill Pain Questionnaire. Measures at baseline, 1, 2, 3, 4 and 6 hours then twice daily for 5 subsequent days (these daily readings were averaged for a daily score). No adverse events.
Notes	Paper gives mean and SEM for normalised data. Patient group is mixed RA/OA.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

van Vliet 1987

Methods	Multicentre RCT of steroid vs placebo. Blinding: Participants and observers blinded. No statistical analysis of baseline variables but appeared comparable. Dropouts: 7 (5%) of 137 recruits were excluded from data analysis as they did not 'fulfill the protocol requirements'. By 84 days the drop out rate was 37% (56% in the control group). Drop out rate at other follow up times is unknown.
Participants	137 participants with RA of knee, aged 27 to 77 years, median disease duration 6.7 years, on stable concurrent systemic treatment. 85% were outpatients. Exclusions: Previous corrective orthopaedic surgery, recent IA steroid injections, pregnancy. The Netherlands.
Interventions	10mg, 20mg and 40mg Rimexolone (in 2ml isotonic injection fluid) vs 2 ml of isotonic injection fluid. Aseptic conditions and local anaesthesia were used following aspiration of all readily accessible synovial fluid.
Outcomes	Included outcomes: Knee flexion (ROM), knee circumference (cm). Excluded outcomes: pain, tenderness and duration of morning stiffness scores (not included as daily rating scale lacked reliability/validity), walking ability (0-3 scale lacks reliability and validity).

Intra-articular steroids and splints/rest for children with juvenile idiopathic arthritis and adults with rheumatoid arthritis (Review)

13

van Vliet 1987 (Continued)

Measures completed at baseline, and Days 7, 28, 56 and 84.
Adverse events: Low (but unspecified) incidence of local and systemic side effects in all groups.

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Weitoft 2003

Methods	RCT of rest vs no rest in wrists injected with IA steroids. Blinding: outcomes assessors. Baseline equivalence: Yes, on demographic variables and major outcome measures. Dropouts: 2 from no-rest group, not prepared to attend 6 month follow up and had no relapse.	
Participants	117 consecutive adults with RA of wrists, aged 28 - 86 years. Only 1 joint could be included. Exclusions: Stenbocker Functional Class 4, major hand deformity, planned hand surgery, daily oral glucocorticoid intake greater to the equivalent of 7.5mg prednisone, IA injection to treated wrist in previous 3 months. Setting: 2 rheumatology clinics in Sweden	
Interventions	48 hours of rest in an elastic wrist orthoses vs normal activity following IA injections with 10mg triamcinolone hexacetonide. DMARDs as per standard management.	
Outcomes	Included outcomes: Primary: Relapse of wrist synovitis (subjects asked to contact clinic is symptoms returned), Secondary outcomes: joint circumference, grip strength (Gripit), Patient Rated Wrist Evaluation (PRWE) Pain (max score = 50) and Function (Max score = 60) scales, wrist extension ROM, all recorded at baseline, 1 week, 3 months and 6 months. No adverse events, 12 subjects in splint group and 8 in normal activity group had DMARDS changed during study period.	
Notes	The published paper contained a Kaplan-Maier curve for relapses and reported no significant difference (p>0.01) on secondary outcomes without giving point estimates and variability data. Weitoft kindly provided information additional to that in the published paper to allow data to be entered into MetaView.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Cats 1979	The outcome measures lacked established reliability and validity. Measures included absent, mild, moderate or severe swelling, tenderness, pain at rest; absent/present temperature, pain on active movement, passive movement and walking and patient and physician rating of clinical change (considerable improvement to much worse).

Study	Reason for exclusion
Chatham 1989	Participants were sampled multiple times ie some joints from one participant were randomised into one treatment group and other joints into a different group and treated as separate N's. Outcome measures: swelling (0-3), pain/tenderness (0-3), ROM and a patient questionnaire.
Kopp 1991	Study of steroid injection into the TMJ joint. The outcomes used for assessing TMJ response are not poolable with those for other joints usually associated with IA injections in arthritis.
Morison 1961	Reported same study as Chandler 1958, but aggregated with a larger population other than those with RA/JA.
Neidel 2002	Prospective follow up study of 50 children who received intra-articular steroid injections for coxitis. Not an RCT.
Petri 1987	Participant population had painful shoulders, not due to arthritis.
Rylance 1980	Not a randomised trial and did not compare steroid with a placebo or other treatment.
Stojanovic 1974	Non-English article which despite efforts was unable to be retrieved.

DATA AND ANALYSES

Comparison 1. IA injections (pooled doses) vs "placebo" - Knees

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Knee flexion (deg)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Knee flexion - 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Knee flexion - 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Knee flexion - 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 Knee flexion - 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Knee circumference (cm)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Knee circumference - 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Knee circumference - 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 Knee circumference - 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.4 Knee circumference - 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Pain - VAS at rest	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Pain - 1 day	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Pain - 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Pain - VAS during activity	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Pain - 1 day	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Pain - 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Pain - McGill	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 McGill - 1 day	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 McGill - 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 1.1. Comparison 1 IA injections (pooled doses) vs "placebo" - Knees, Outcome 1 Knee flexion (deg).

Study or subgroup	Injection		Placebo		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
1.1.1 Knee flexion - 1 week						
van Vliet 1987	94	120.8 (19)	32	116.4 (24.8)	4.37[-5.04,13.78]	
1.1.2 Knee flexion - 2 to 6 weeks						
van Vliet 1987	88	121.3 (19.6)	25	114.2 (18.9)	7.13[-1.33,15.59]	
1.1.3 Knee flexion - 7 to 11 weeks						
van Vliet 1987	72	120 (20)	18	120.3 (15.7)	-0.26[-8.86,8.34]	
1.1.4 Knee flexion - 12 to 24 weeks						
van Vliet 1987	65	117.1 (22.4)	14	118.7 (21.4)	-1.58[-14.05,10.89]	
					-100 -50 0 50 100	Favours treatment Favours control

Analysis 1.2. Comparison 1 IA injections (pooled doses) vs "placebo" - Knees, Outcome 2 Knee circumference (cm).

Study or subgroup	Injection		Placebo		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
1.2.1 Knee circumference - 1 week						
van Vliet 1987	64	38.2 (3.3)	32	39.5 (3)	-1.3[-2.61,0.01]	
1.2.2 Knee circumference - 2 to 6 weeks						
van Vliet 1987	68	38.6 (3.2)	25	39.7 (3.6)	-1.1[-2.7,0.5]	
					-10 -5 0 5 10	Favours treatment Favours control

Analysis 1.3. Comparison 1 IA injections (pooled doses) vs "placebo" - Knees, Outcome 3 Pain - VAS at rest.

Analysis 1.4. Comparison 1 IA injections (pooled doses) vs "placebo" - Knees, Outcome 4 Pain - VAS during activity.

Analysis 1.5. Comparison 1 IA injections (pooled doses) vs "placebo" - Knees, Outcome 5 Pain - McGill.

Comparison 2. Comparison of doses (Van Vliet Daskalopoulou) - Knees

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Knee flexion (deg)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 10mg v placebo at 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 10mg v placebo at 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 10mg v placebo at 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 10mg v placebo at 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.5 20mg v placebo at 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.6 20mg v placebo at 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.7 20mg v placebo at 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.8 20mg v placebo at 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.9 40mg v placebo at 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.10 40mg v placebo at 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.11 40mg v placebo at 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.12 40mg v placebo at 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Knee circumference	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 10mg v placebo at 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 10mg v placebo at 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.3 10mg v placebo at 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.4 10mg v placebo at 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.5 20mg v placebo at 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.6 20mg v placebo at 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.7 20mg v placebo at 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.8 20mg v placebo at 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.9 40mg v placebo at 1 week	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.10 40mg v placebo at 2 to 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.11 40mg v placebo at 7 to 11 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.12 40mg v placebo at 12 to 24 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Comparison of doses (Van Vliet Daskalopoulou) - Knees, Outcome 1 Knee flexion (deg).

Study or subgroup	IA injection		Placebo		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
2.1.1 10mg v placebo at 1 week						
van Vliet 1987	32	121.4 (17.2)	32	116.4 (24.8)		5[-5.46,15.46]
2.1.2 10mg v placebo at 2 to 6 weeks						
van Vliet 1987	29	120.7 (19.9)	25	114.2 (18.9)		6.5[-3.86,16.86]
2.1.3 10mg v placebo at 7 to 11 weeks						
van Vliet 1987	22	117.2 (22.2)	18	120.3 (15.7)		-3.1[-14.88,8.68]
2.1.4 10mg v placebo at 12 to 24 weeks						
van Vliet 1987	21	114.7 (24.7)	14	118.7 (21.4)		-4[-19.4,11.4]
2.1.5 20mg v placebo at 1 week						
van Vliet 1987	32	117.5 (22.8)	32	116.4 (24.8)		1.1[-10.57,12.77]
2.1.6 20mg v placebo at 2 to 6 weeks						
van Vliet 1987	30	118.2 (22.8)	25	114.2 (18.9)		4[-7.02,15.02]
2.1.7 20mg v placebo at 7 to 11 weeks						
van Vliet 1987	26	118 (20.6)	18	120.3 (15.7)		-2.3[-13.04,8.44]
2.1.8 20mg v placebo at 12 to 24 weeks						
van Vliet 1987	23	115.8 (23.5)	14	118.7 (21.4)		-2.9[-17.66,11.86]
2.1.9 40mg v placebo at 1 week						

Favours treatment -100 -50 0 50 100 Favours control

Analysis 2.2. Comparison 2 Comparison of doses (Van Vliet Daskalopoulou) - Knees, Outcome 2 Knee circumference.

Comparison 3. Splints/rest plus IA injection vs IA injection alone - Wrists

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of relapses	1	117	Odds Ratio (M-H, Fixed, 95% CI)	2.27 [1.02, 5.03]
2 Pain (Patient Rated Wrist Evaluation)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 1 week	1	117	Mean Difference (IV, Fixed, 95% CI)	-2.0 [-5.64, 1.64]
2.2 3 months	1	99	Mean Difference (IV, Fixed, 95% CI)	1.10 [-3.92, 6.12]
2.3 6 months	1	81	Mean Difference (IV, Fixed, 95% CI)	-4.1 [-9.26, 1.06]
3 Wrist function (Patient Rated Wrist Evaluation)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 1 week	1	117	Mean Difference (IV, Fixed, 95% CI)	-1.5 [-5.96, 2.96]
3.2 3 months	1	99	Mean Difference (IV, Fixed, 95% CI)	2.20 [-4.27, 8.67]
3.3 6 months	1	81	Mean Difference (IV, Fixed, 95% CI)	-1.90 [-8.98, 5.18]
4 ROM - Wrist	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.1 1 week	1	117	Mean Difference (IV, Fixed, 95% CI)	-0.90 [-7.36, 5.56]
4.2 3 months	1	99	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-11.24, 11.04]
4.3 6 months	1	81	Mean Difference (IV, Fixed, 95% CI)	-9.30 [-19.40, 0.80]
5 Wrist circumference	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 1 week	1	117	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-2.40, 1.40]
5.2 3 months	1	99	Mean Difference (IV, Fixed, 95% CI)	0.5 [-2.49, 3.49]
5.3 6 months	1	81	Mean Difference (IV, Fixed, 95% CI)	-2.7 [-5.97, 0.57]
6 Grip strength - Grippit	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 Peak value 1 week	1	117	Mean Difference (IV, Fixed, 95% CI)	4.20 [-15.08, 23.48]
6.2 Peak value 3 months	1	99	Mean Difference (IV, Fixed, 95% CI)	-6.60 [-29.42, 16.22]
6.3 Peak value 6 months	1	81	Mean Difference (IV, Fixed, 95% CI)	-9.70 [-39.65, 20.25]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.4 10 second mean force 1 week	1	117	Mean Difference (IV, Fixed, 95% CI)	1.5 [-15.20, 18.20]
6.5 10 second mean force 3 months	1	99	Mean Difference (IV, Fixed, 95% CI)	-9.40 [-29.51, 10.71]
6.6 10 second mean force 6 months	1	81	Mean Difference (IV, Fixed, 95% CI)	-8.60 [-34.04, 16.84]

Analysis 3.1. Comparison 3 Splints/rest plus IA injection vs IA injection alone - Wrists, Outcome 1 Number of relapses.

Analysis 3.2. Comparison 3 Splints/rest plus IA injection vs IA injection alone - Wrists, Outcome 2 Pain (Patient Rated Wrist Evaluation).

Analysis 3.3. Comparison 3 Splints/rest plus IA injection vs IA injection alone - Wrists, Outcome 3 Wrist function (Patient Rated Wrist Evaluation).

Analysis 3.4. Comparison 3 Splints/rest plus IA injection vs IA injection alone - Wrists, Outcome 4 ROM - Wrist.

Analysis 3.5. Comparison 3 Splints/rest plus IA injection vs IA injection alone - Wrists, Outcome 5 Wrist circumference.

Analysis 3.6. Comparison 3 Splints/rest plus IA injection vs IA injection alone - Wrists, Outcome 6 Grip strength - Grippit.

ADDITIONAL TABLES

Table 1. Data from Chakravarty - response curve values

Variable	No rest group	Rest group	P-value
Pain - VAS	-2.10	-4.26	<0.0001
Stiffness - VAS	-0.48	-3.44	<0.0001
Knee circumference - cm	-15.7	-18.5	<0.02
Walking time - secs	-12.6	-18.2	<0.0001

APPENDICES

Appendix 1. MEDLINE search strategy

TOPIC SEARCH STRATEGY

- 1 exp arthritis, rheumatoid/ (68907)
- 2 (felty\$ adj2 syndrome).tw. (525)
- 3 inflammatory arthritis.tw. (1065)
- 4 (sjogren\$ adj2 syndrome).tw. (6907)
- 5 still\$ disease.tw. (850)
- 6 (arthritis adj2 rheumat\$).tw. (43182)
- 7 (juvenile adj2 arthritis).tw. (4122)
- 8 bechterew\$ disease.tw. (267)
- 9 or/1-8 (78631)
- 10 exp Steroids/ (484444)
- 11 exp Glucocorticoids/ (109266)
- 12 (Methylprednisolone or Prednisolone or prednisone or Triamcinolone or

Triamcinolone acetate or Beclomethasone).sh,rn. (55214)
 13 exp Adrenal Cortex Hormones/ (131848)
 14 (corticoid\$ or corticosteroid\$ or hydrocortisone or glucocorticoid\$ or
 steroid\$).tw. (178523)
 15 or/10-15 (585755)
 16 Injections, Intra-Articular/ (3077)
 17 (intra-articular injection\$ or intraarticular injection\$ or
 intra-articular therap\$ or intraarticular therap\$).tw. (1509)
 18 16 or 17 (3795)
 19 15 and 18 (1414)
 20 9 and 19 (428)

NB: The subset of articles which examined resting or splinting joints following IA injections were drawn from this search.

WHAT'S NEW

Date	Event	Description
30 June 2008	Amended	Converted to new review format. CMSG ID: A012-R

CONTRIBUTIONS OF AUTHORS

MW co-developed the review protocol, conducted the searches, selected trials for the review, extracted data, analysed and interpreted data, wrote the review.

DG co-developed the review protocol, selected trials for the review, extracted data, analysed and interpreted data, and contributed the methodological expertise.

DECLARATIONS OF INTEREST

None known

SOURCES OF SUPPORT

Internal sources

- The Children's Hospital at Westmead, Australia.

External sources

- No sources of support supplied

NOTES

Note - protocol title was originally 'Splints/Rest in combination with intra-articular steroid injections for treating children with arthritis'.

INDEX TERMS

Medical Subject Headings (MeSH)

*Splints; Arthritis, Juvenile [drug therapy] [therapy]; Arthritis, Rheumatoid [drug therapy] [*therapy]; Combined Modality Therapy [methods]; Glucocorticoids [*administration & dosage]; Injections, Intra-Articular; Randomized Controlled Trials as Topic

MeSH check words

Adult; Child; Humans