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Injection Therapy for Subacute and Chronic Benign Low Back Pain

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Study Design. The Medline and Embase databases containing randomized controlled trials of injection therapy published to 1998 were systematically reviewed.

Objectives. To evaluate the effectiveness of injection therapy with anesthetics, steroids, or both in patients with low back pain persisting longer than 1 month.

Methods. Two reviewers independently assessed the trials for the quality of their methods. The primary outcome measure was pain relief. Subgroup analyses were performed between trials with different control groups (placebo and active injections), with different injection sites (facet-joint, epidural, and local injections), and with timing of outcome measurement (short- and long-term). Within the resulting 12 ($2 \times 3 \times 2$) subcategories of studies, the overall relative risks and corresponding 95% confidence intervals were estimated, using the random effects model of DerSimonian and Laird. In the case of trials using active injections as a control, the results were not pooled.

Results. This review included 21 randomized trials. All the studies involved patients with low back pain persisting longer than 1 month. Only 11 studies compared injection therapy with placebo injections (explanatory trials). The methodologic quality of many studies was low: Only eight studies had a methodologic score of 50 points or more. There were only three well-designed explanatory clinical trials: one on injections into the facet joints with a short-term relative risk of 0.89 (95% confidence interval = 0.65–1.21) and a long-term relative risk of 0.90 (95% confidence interval = 0.69–1.17), one on epidural injections with a short-term relative risk of of 0.94 (95% confidence interval = 0.76–1.15) and a long-term relative risk of 1.00 (95% confidence interval = 0.71–1.41), and one on local injections with a long-term relative risk of 0.79 (95% confidence interval = 0.65–0.96). Within the six subcategories of explanatory studies, the pooled relative risks were as follows: facet joint, short-term: relative risk = 0.89 (95% confidence interval = 0.65–1.21); facet joint, long-term: relative risk = 0.90 (95% confidence interval = 0.69–1.17); epidural, short-term: relative risk = 0.93 (95% confidence interval = 0.79–1.09); epidural, long-term: relative risk = 0.92 (95% confidence interval = 0.76–1.11); local, short-term: relative risk = 0.80 (95% confidence interval = 0.40–1.59); and local, long-term: relative risk = 0.79 (95% confidence interval = 0.65–0.96).

Conclusions. Convincing evidence is lacking regarding the effects of injection therapy on low back pain. Additional well-designed explanatory trials in this field are needed. [Key words: facet denervation, injections, low back pain, review, clinical trials] **Spine 2001;26:501–515**

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The burden of chronic low back pain on society is enormous in terms of both patient suffering and cost (*Quebec Task Force* on Spinal Disorders, 1987). Numerous treatments have been advocated, but not many have proved to be effective (Bell, 1984; Deyo, 1984). Injection with anesthetics, steroids, or both is one of the treatment methods used to treat patients with chronic low back pain, which needs evaluation with respect to the effectiveness for short- and long-term pain relief.

Injection therapy is applied at different locations. Injections into facet joints have been presented as treatment and also as a diagnostic test for the lumbar facet-joint syndrome. There are no objective criteria for this syndrome. The clinical diagnosis is based on the presence of localized lumbar pain, which may radiate to the posterior aspect of the thigh and be relieved by an injection of corticosteroids and local anesthetic (Mooney(b), 1987; Mooney(a); Robertson, 1976).

Injections can be given intra- or periarticularly. Epidural anesthesia involves injection of a solution of local anesthetic into the epidural space. The anesthetic acts in two places. It diffuses across the dura into the subarachnoid space, where it acts on nerve roots and the spinal cord. The drug also diffuses into the paravertebral area through the intervertebral foramens, producing, in essence, multiple paravertebral nerve blocks. The subarachnoid space is the more important site of action (Ritchie, 1990).

Local injection therapy is a badly defined term. Injections can be administered for several syndromes. In the reviewed studies, injections were used at many locations. Sometimes the anesthetic was injected into the iliolumbar ligaments, but injections into tender points, trigger points, or acupuncture points and intradiscal injections also are mentioned in the reports. Sometimes it is not even clear into which tissue the anesthetic has been injected.

Many controversies exist regarding the effectiveness of injection therapy. It is not clear why an injection with a short-acting anesthetic would provide prolonged pain relief. Furthermore, randomized controlled studies on the effectiveness of injection therapy have yielded controversial results. Evidence for both short- and long-term effectiveness is lacking.

Recent reviews have shown contradictory results, although there has been considerable overlap between the trials included in these reviews (Koes et al, 1995; Watts et al, 1995). Koes et al reviewed 12 randomized clinical trials on the efficacy of epidural steroid injections for low

back pain and sciatica. One half of the trials reported positive outcomes from epidural steroid injections, and the other half reported negative outcomes. Critical assessment of the methods used in these trials showed flaws in the design for most of the studies, although there appeared to be no relation between the methodologic quality of the trials and the reported outcomes. Koes et al concluded that the efficacy of epidural injections has not yet been established.

Watts et al performed a meta-analysis of 11 placebo-controlled trials on the efficacy of epidural steroid injections in the treatment of sciatica, nine of which also were considered by Koes. The methodologic quality of the trials was considered generally to be good for the five studies that scored the maximum number of points. Improvement of at least 75% or reduction in pain was considered to be a clinically useful response. With respect to short-term pain relief (1 to 60 days), the pooled odds ratio (OR), based on 10 trials, was 2.61 (95% confidence interval [CI] = 1.80–3.77), whereas for long-term pain relief (12 weeks to 1 year), the pooled odds ratio, based on 5 trials, was 1.87 (95% CI = 1.31–2.68). Watts et al concluded that epidural steroid injections are effective in the management of patients with sciatica.

The current authors decided to perform another systematic review of randomized clinical trials on the efficacy of injection therapy in patients with low back pain. This review differed from the previous reviews because 1) it did not restrict itself to epidural steroid injections, but also considered epidural injections with anesthetics and other injection sites such as facet joints and local sites; and 2) it was restricted to randomized clinical trials, which included patients with low back pain persisting longer than 1 month. This inclusion criterion was used to reduce the chance of spontaneous recovery.

There is an 80% to 90% probability that patients with low back pain will recover spontaneously within 3 months, with the chance of recovery diminishing as time passes (Garvey et al, 1989). In a clinical trial, a high spontaneous success rate in the control group is "noise" that may obscure the efficacy of active treatment, making the trial inefficient. This can be illustrated by an example. Supposing that active therapy will cure 50% of the patients who will not recover spontaneously, if the spontaneous recovery rate is 30% in the control group, then 65% (30% + [0.5 × 70%]) of the patients in the experimental group will recover, yielding a difference of 35%. If the spontaneous recovery rate in the control group is 10%, then 55% (10% + [(0.5 × 90%]) of the patients in the experimental group will recover, yielding a difference of 45%. Therefore, it is easier to show an effect by keeping spontaneous recovery rates low (Knipschild, 1991). One way to achieve low recovery rates might be to restrict the study population to patients with low back pain persisting longer than 1 month. Experience teaches that the longer the duration of low back pain in the control group, the smaller the proportion of patients with a natural tendency to improve.

■ Methods

Inclusion Criteria for Studies

Types of Studies. To be included in this review, studies had to meet three criteria. First, the study design had to be a randomized clinical trial. Second, the treatment had to include injection therapy for pain relief, although additional treatments were allowed. Third, the patients had to have benign chronic low back pain with symptoms persisting longer than 1 month.

Types of Participants. The study population, as defined by the inclusion and exclusion criteria for this review, consisted of patients with subacute and chronic low back pain (*i.e.,* lasting longer than 1 month).

Types of Interventions. Injection therapy was studied at three injection sites: facet joints, epidural sites, and local sites.

Types of Outcome Measures. The percentage of patients with pain relief was considered to be the most important outcome measure. Pain is evaluated on both a short-term (<6 weeks) and long-term (>6 weeks) basis. Other outcome measures other than pain used in the trials also were listed.

Search Strategy for Identifying Studies. Medline and Embase searches of papers published over the period 1966–1998 were conducted. The keywords used were low back pain, back, neck, injections, chemonucleolysis, rhizotomy, facet denervation, thermolesion, trial, random, controlled, and review. Citation tracking was performed until no new studies were found. Abstracts and unpublished studies were not included. English, French, German, Dutch, and Nordic languages were considered eligible for retrieval purposes.

Review Methods.

Study Selection. Studies were selected if they met the three inclusion criteria.

Data Extraction. A standardized form was used to extract the relevant data on the methods used, participants, interventions, outcome measures used and timing of outcome measurement, reported side effects, and the main results.

Data Analysis. The proportion of patients with pain relief was used as the primary outcome measure in this review. Raw data on the number of patients with pain relief and the total number of patients in each treatment group were entered into Review Manager. The included trials were subdivided according to the injection site studied (facet-joint *vs* epidural *vs* local injection), the type of trial (explanatory *vs* pragmatic), and timing of the outcome measurement (within 6 weeks of intervention *vs* 6 weeks after intervention). A trial was designated as explanatory if the control group had a placebo injection, and as pragmatic if the control groups had another type of active injection. Within the resulting 12 (3 × 2 × 2) subcategories of studies, the overall relative risks and corresponding 95% confidence intervals were estimated, using a random effects model designed by DerSimonian and Laird. In the case of pragmatic studies, the results were not pooled.

Methodologic Quality. The methodologic quality of the studies under review was scored by using a criteria list (ter Riet et al, 1990). The following table specifies the items evaluated:

- A selection and restriction (4 points)
- B treatment allocation (15 points)
- C study size (12 points)
- D prognostic comparability (10 points)
- E dropouts (12 points)
- F loss to follow-up assessment (10 points)
- G description of intervention (5 points)
- H extra treatments (2 points)
- I blinding of patients (4 points)
- J blinding of physician (4 points)
- K blinding of observer (4 points)
- L outcome measures (5 points)
- M timing of outcome measurements (6 points)
- N side effects (2 points)
- O analysis and presentation of data (5 points)

The criteria were based on generally accepted principles of intervention research (Meinert, 1986; Pocock, 1991). Studies could earn points for each criterion met. The maximum score was 100 points. The quality of the study methods was scored independently by two reviewers (R.dB., H.dV.). In a meeting, the reviewers reached consensus on the small number of criteria (5%) about which they disagreed.

Items Used to Assess Methodologic Quality and Justification of Weights.

Internal Validity. More than half of the points could be earned with items on the criteria list that were pivotal for ensuring validity.

Treatment Allocation (B). Randomization is essental to ensure balance for any unknown or known prognostic factors so that unbiased comparisons between intervention groups can be made. Information on the randomization procedure had to be given in sufficient detail to enable the reviewers to judge whether the procedure was foolproof in concealing the assigned treatment from the referring clinicians.

Prognostic Comparability (D). The maximal score was assigned to publications wherein the distribution of seven baseline characteristics (age, gender, duration of symptoms, baseline scores for outcome measures, concomitant medication, previous operations, and effectiveness of prognostic blocking) was similar and clearly presented for intervention groups. The number of points on this item was determined by the number of characteristics for which the intervention groups were comparable multiplied by 10/7.

Blinding of the Patient, Therapist, and Observer to Treatment Allocation (I,J,K). Half of the maximal score (6 points) could be earned by attempts to blind the patient, therapist, and/or observer, for example, by using a placebo injection with the control group, or by letting an observer, who was unaware of the treatment allocation, assess clinical outcome. The more subjective the measurement of clinical outcome is, the more important masking techniques become. All 12 points were assigned when the authors had checked whether the blinding had succeeded.

Number of Dropouts and Losses to Follow-Up Assessment (E,F). Information on the flow of participants had to include the number of participants eligible, randomized, treated, and completing or failing to complete the trial by intervention group. "Dropouts" were patients who were randomized but did not complete the intervention, such as noncompliant patients and those experiencing serious adverse effects. "Losses to follow-up assessment" referred to patients who finished treatment but did not return for all the measurements of clinical outcome. Trials scored well if the numbers of dropouts and losses to follow-up assessment were rather small (dropouts less than 5%, losses to follow-up assessment less than 10%) or the reasons were not related to clinical outcome. In these situations, the resulting bias was regarded as small and as not seriously affecting the results of the trial.

Extra Treatments (H). Cointerventions had to be reported, and extra treatments with a potential beneficial effect on clinical outcome had to be comparable in both intervention groups.

Relevance. Items such as selection and restriction (A), intervention (G), outcome measures (L), timing of outcome measurements (M), and side effects (N) refer to relevance of the trial to clinical practice.

Description of Inclusion and Exclusion Criteria (A). This item was considered to be important because it informs the reader about the type of patients to whom the study results apply and the homogeneity of the study population.

Intervention (G). Interventions had to be described in detail in terms of dose, technique, route, and frequency of administration.

Outcome Measurements (L). Measures for assessing and recording a patient's progress had to be defined clearly. The score on the "outcome measures" item depended on the number of relevant measures (pain, global improvement, functional physical status, medical consumption, functional status). For example, a study having six outcome measurements, of which only one was considered relevant, the score was calculated as $1/6 \times 5 = 0.8$ points.

Timing of Outcome Measurements (M). The timing of outcome measurements had to be stated explicitly so short-term and long-term effects could be distinguished.

Side Effects (N). Accurate reporting of side effects according to treatment group was considered to be necessary for evaluating the safety of the intervention(s) under study.

Statistical Approaches. Although many statistical aspects could be considered, the checklist for the current study focused on study size (C) as well as analysis and presentation of data (O).

Study size (C). A maximal score was allocated in cases of adequate sample size. Trials with insufficient sample size may cause potentially useful new therapies to be ignored (Type 2 error or β error). The power of the study (*i.e.,* the probability of detecting a postulated level of effect) is too low. In these situations, the lack of statistical significance does not allow the conclusion that the intervention under study was not effective.

Analysis and interpretation of data (O). With respect to the presentation of data, a trial could score well if the data were presented in a way that allowed a number of simple effect measures (*e.g.,* percentage of patients with pain improvement)

to be compared by the reviewers and statistical analyses to be checked. Furthermore, the scoring list addressed the question whether the primary analysis was performed according to the intention-to-treat principle, meaning that the analysis included all the participants and their follow-up results in the intervention groups to which they were assigned initially. Such analysis was preferred because it does not violate the comparability of baseline characteristics and relates to actual clinical practice.

■ Results

The search strategy yielded 40 papers.[1,3–9,11,12,14–19,22–27,29,32,33,35,37,38,41–50,52,53] After detailed reading, 19 studies were excluded: Six of these studies appeared to be nonrandomized.[12,14,43–45,52] In one study, an anesthetic agent was injected into the wound during surgery,[29] and in seven studies, either patients with acute problems (<1 month) were included[11,17,35,48,50] or the duration of the reported problems was not described.[19,53] Five studies[24,25,32,37,38] fell outside the domain of this review. The two reports by Lillius et al[22,23] described the same study, so both were used to assess the methodologic quality of the study. The report by Matthews et al[27] described several trials, one concerning local injection and another about one epidural injection.

Eventually, 21 papers describing 21 trials were included for review. The characteristics of the included studies are described in Table 1. The excluded studies and the reasons for their exclusion are described in Table 2.

Methodologic Quality of the Included Studies

The methodologic quality of the studies varied from 23 to 83 out of 100 possible points (Table 3). Most of the studies gave an adequate description of the intervention, the timing of the outcome, and the side effects. However, on all other items most of the studies received less than 50% of the maximum score. Initially, there was a 5% rate of disagreement between the two independent reviewers, mainly caused by reading and/or interpretation errors. In a consensus meeting, the differences were resolved. The scores on individual items are tabulated in Tables 4 and 5.

Study Population

The study population, as defined by the inclusion and exclusion criteria, consisted of patients with chronic low back pain. Additional characteristics differed per study, especially with respect to duration of reported problems, radicular symptoms, and operation. Epidural injections were used mainly for patients with sciatica. Exceptions were the studies of Glynn et al (1988) and Serrao et al (1992). Facetal joint injections were used with patients suspected of having the facet-joint syndrome. Carette et al (1991) tried to specify the diagnosis by including only patients who responded to injection of lidocaine into the facetal joint and showed pain relief of at least 50%. The trials on the effect of local injections included patients with iliac crest syndrome (Collée et al, 1991),myofascial syndrome (Hameroff et al, 1981), nonspecified low back pain (Garvey et al, 1989; Mathews et al, 1987; Ongley et al, 1987), or mechanical low back pain (Serrao et al, 1992).

Interventions

Eleven studies were of an explanatory nature, comparing an experimental therapy with a placebo injection (*e.g.*, saline or procaine). The remainder of the studies compared two active agents and are referred to as pragmatic studies. A diversity of drugs was used in the reviewed studies. These drugs can be divided roughly into anesthetics, steroids, benzodiazepines (midazolam), opioids, and sclerosants. Apart from the medication used, the volume, the dose, and site of injection also varied. Moreover, there were differences between the studies with respect to the injection techniques. Some of the epidural injections were caudal (*i.e.*, through the sacral hiatus (Bush and Hillier, 1991).

Effect Measurements

In all the studies, pain was considered to be the most important outcome measure. Pain usually was measured on a visual analogue scale or an ordinal scale, but often was dichotomized into satisfactory pain relief or no pain relief for the final outcome. Many studies assessed only

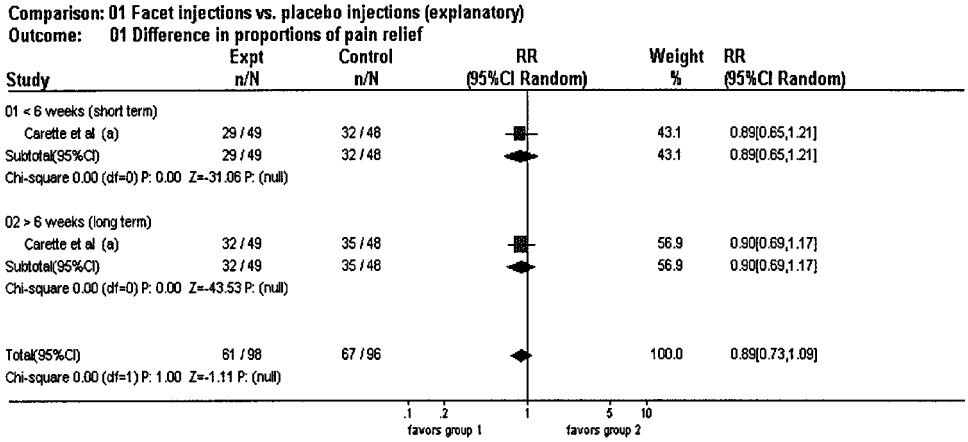

Figure 1. n = number of patients without pain relief.

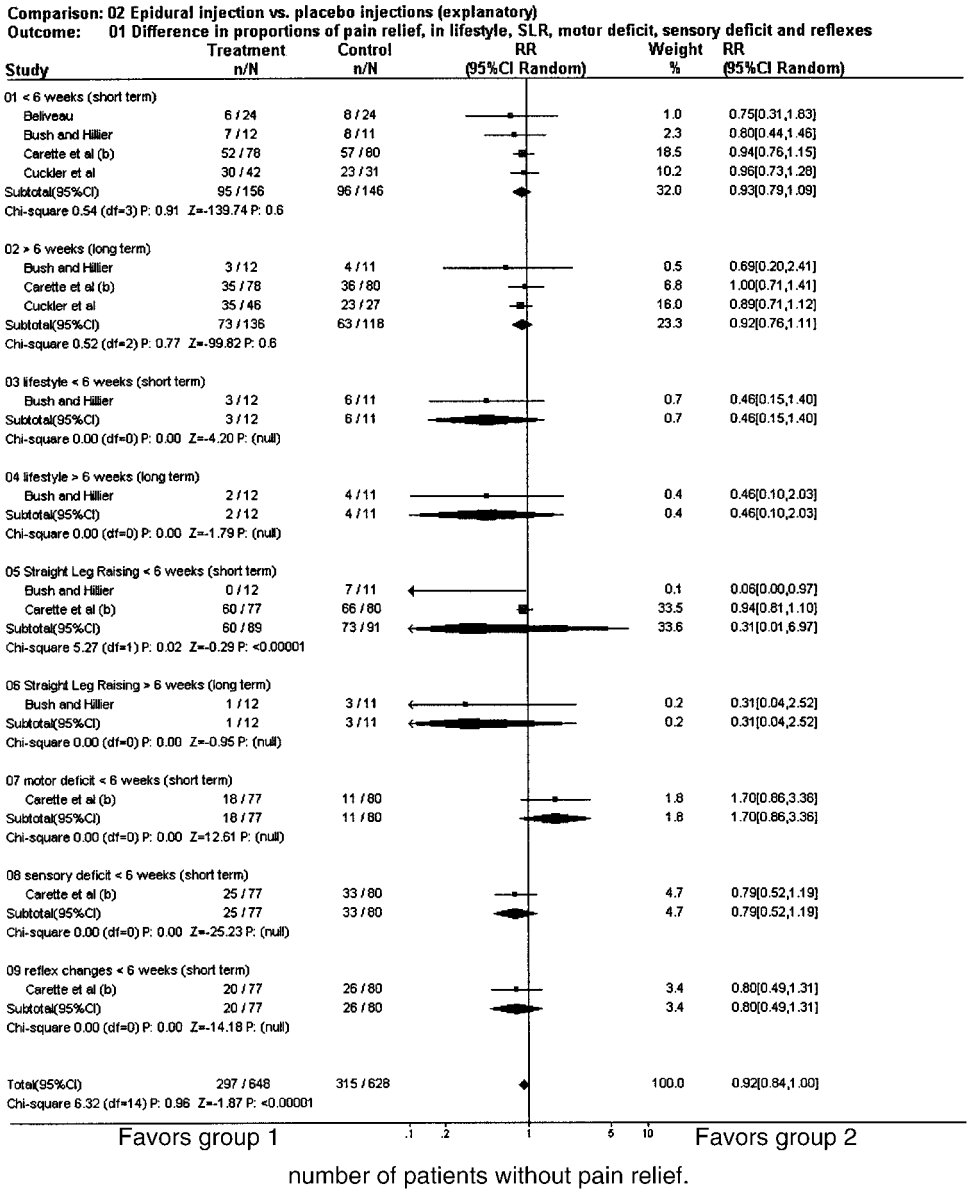

Figure 2. n = number of patients without pain relief.

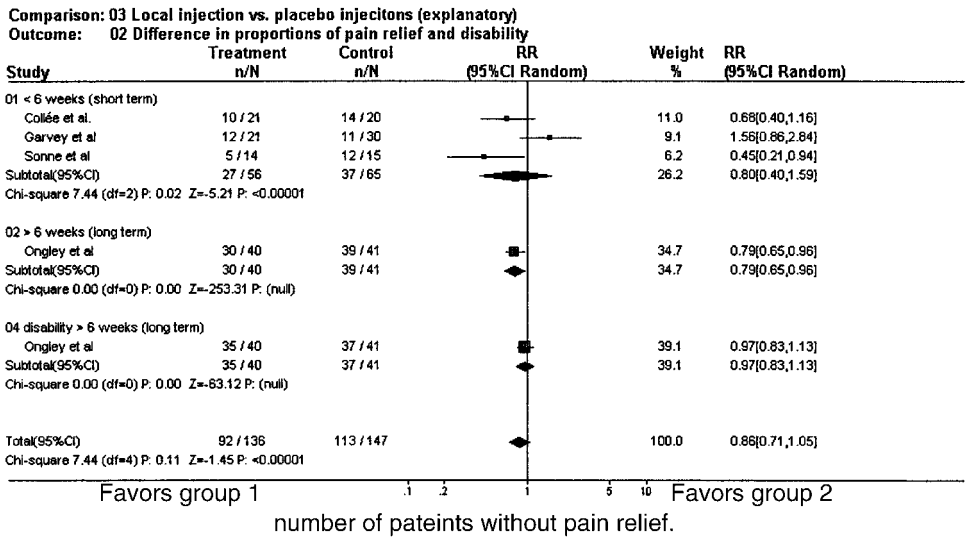

Figure 3. n = number of patients without pain relief.

Table 1. Characteristics of Included Studies

Study	Methods	Participants	Interventions	Outcomes	Notes	A*
Beliveau[1]	Patients were allocated alternately to the treatment groups.	Department of Rheumatology and Physical Medicine, St Thomas' Hospital, London, UK. 48 patients with unilateral sciatica. Mean age: 40.6; age range: 19–71, male/female: 36/12.	Epidural injections: 1. 2 mL (80 mg) methylprednisolone + 40 mL of procaine 0.5% (n = 24). 2. 42 mL of procaine 0.5% (n = 24).	Timing: 1 week after injection. Outcome measures: change in pain.	Side effects: mild headache and dizziness (n = 10). Theca penetration (n = 2). Methodologic score: 23.8%.	C
Breivik et al[3]	Randomized controlled trial. Double blind. Randomization according to a list of random numbers.	Departments of Anesthesiology and Neurology, University of Oslo, Akershus Central Hospital, Norway, 35 patients with incapacitating chronic low back pain and sciatica. Diagnoses based on radiculography: arachnoiditis (n = 8), prolapsed disc (n = 8), no abnormality (n = 11), inconclusive findings (n = 5). Duration: several months to several years. Experimental group: age range: 30–63; male/female: 8/8. Placebo group: age range: 30–61: male/female: 9/10.	Caudal epidural injection: 1. 20 mL bupivacaine 0.25% with 80 mg depotmethylprednisolone (n = 16). 2. 20 mL bupivacaine 0.25% followed by 100 mL saline (n = 19). Frequency: up to three injections at weekly intervals.	Timing: not mentioned. Outcome measures: 1. Pain relief: considerable relief was defined as significant diminution of pain and/or paresis to a degree that enabled return to work. 2. Objective improvement: hypo- or anesthesia, Lasegue's test, paresis, spinal reflexes, and sphincter disorders.	If there was no improvement 3 weeks after the last injection, up to three injections of the alternative type was given. Score: 54.1%.	A
Bush and Hillier[4]	Randomized controlled trial. Double blind. Statistical tests: Wilcoxon test for changes in lifestyle and VAS scores. 28 patients were randomized; only 23 patients were entered into the study. Withdrawals because of deterioration of symptoms: 1 in experimental group, 4 in control group.	Rheumatology Department of the Royal Free Hospital, London, UK. 23 patients with lumbar nerve root compromise. Duration of pain >1 month. Experimental group: mean age: 38; age range: 23–71; male/female: 10/2. Control group: mean age: 37; age range: 26–52; male/female: 5/6. Mean duration (range) in experimental group: 5.8 months (1–13 months) and in control group 4.7 months (1–12).	Epidural injections: 1. 25 mL (80 mg) triamnicolone acetonide + 0.5% procaine hydrochloride (n = 12). 2. 25 mL normal saline (n = 11). Two caudal injections, the first after admission to the trial and a second after 2 weeks.	Timing: at 4 weeks and at 1 year. Outcome measures: 1. effect on lifestyle. 2. back and leg pain (VAS) (change of VAS score >20 was used as positive criterion in this review). 3. angle of positive SLR.	At baseline, the intervention groups differed with respect to SLR ability, with less mobility impairment in the control group. No major side effects were reported. Score: 39.9%.	B
Carette et al (a)[6]	Randomized controlled trial. Randomization by random numbers generation, balancing after every 8 patients. Stratification for receiving disability compensation or not. Blinding of treating physician. Intention-to-treat analysis. Predefined sample size calculations. Statistical tests: chi-square, Fisher's exact test, Wilcoxon test, ANCOVA	Centre Hospitalier de l'Université Laval, Quebec City, Canada. 101 patients with pain originating in the facetal joints and >50% pain reduction (on VAS) after injection with lidocaine were entered into the trial. Exclusion criteria: patients with pain of mechanical causes, previous injection into the facet joints, low back surgery, abnormal results in neurologic examination. After randomization 4 patients were excluded because of sacroiliitis (n = 1) and pain duration <6 months (n = 3). Experimental group (n = 49): mean age 42.5, male 51%. Control group (n = 48): mean age 43, male 58%. Duration of pain >6 months. Mean duration of pain: experimental group: 18 months, control group: 24 months.	Facet joint injections: 1. methylprednisolone acetate (20 mg) 1 mL + 1 mL saline (n = 49). 2. isotonic saline 2 mL (n = 48).	Timing: at 1, 3, and 6 months after randomization and treatment. Outcome measures: 1. self-rating of overall effect ranging from very marked improvement to very marked deterioration. 2. pain at rest and on lumbar flexion and extension (not reported). 3. functional status by modified version of the Sickness Impact Profile (NS on short and long term). 4. the distance from the finger to the floor in maximal forward flexion (NS on short and long term).	Side effects: none other than transient local pain at the injection sites. Score: 83.1%.	A

(Table continues)

short-term effects. Of the 21 clinical trials included, 19 studies presented raw data on the proportions of patients with pain relief. Hameroff et al (1981) and Lilius et al (1989) presented mean pain scores and no proportions.

Effectiveness of Injection Therapy

With respect to facet-joint injections, Carette et al (a) (1991) reported that they did not find significant differences in proportions of pain improvement between cor-

Table 1. Continued

Study	Methods	Participants	Interventions	Outcomes	Notes	A*
Collée et al.[7]	Random allocation. Double blind (patient, physician, and observer). Statistical tests: chi-square, Mann-Whitney *U*, multiple-regression analysis.	Department of Rheumatology and Clinical Epidemiology, University Hospital Leiden, The Netherlands. 41 patients with iliac crest pain syndrome. Excluded are sciatica, ankylosing spondylitis, malignancies, infection, spondylolisthesis, degenerative disc disease, fibromyalgia. Median duration of pain in rheumatology setting 8 years, and in GP setting 18 days. Experimental group: mean age 43 ± 12, 38% males, 57% rheumatology setting. Control group: mean age 42 ± 14, 20% males, 60% rheumatology setting.	Local injections 1. 5 mL lignocaine 0.5% (n = 21). 2. 5 mL isotonic saline (n = 20).	Timing: baseline, 10 min after injection, 7, 14 days, and 2 months after injection. Outcome measures: 1. pain score on VAS. 2. hours of low back pain per day (not significantly different: data not shown). 3. duration and intensity of morning stiffness (not significantly different: data not shown). 4. use of medication (not significantly different: data not shown). 5. palpation for tenderness of the medial part of the iliac crest (not significantly different: data not shown). 6. movements of the lumbar spine and hips to reproduce pain (not significantly different: data not shown).	Side effects: painful injection: experimental (n = 2), control (n = 3). Temporary paraesthesia near injection site: experimental (n = 2), control (n = 2). Nausea: experimental (n = 2), control (n = 1). Score: 47.4%.	B
Cuckler et al[8]	Randomized controlled trial. Double blind. Statistical tests used were: chi-square, Student *t* test, Kruskall-Wallis nonparametric ANOVA.	Pennsylvania. 73 patients with clinical and radiographic evidence of nerve root compression. In steroid group: mean age: 48.5, male/female: 20/22, mean duration of HNP 14.5 months and of spinal stenosis 36.6 months. In control group: mean age: 49.5, male/female: 17/14, mean duration of HNP 13.1 months and of spinal stenosis 29.4 months.	Epidural injections: 1. 2 mL (80 mg) methylprednisolone acetate +5 mL of procaine (1%) (n = 42). 2. 2 mL of saline + 5 mL of procaine (1%) (n = 31).	Timing: at 24 hours after injection and long-term success at 13–30 months. Outcome measures: 1. subjective improvement of 75% or more was defined as success.	If improvement at 24 hours after injection was <50%, a second injection of methylprednisolone acetate was given. These patients were designated as having a failed result. Side effects not reported. Skewed randomization. Long-term outcome data do not add up to initial group totals. Score: 57.1%.	B
Dallas et al[9]	Randomized controlled trial. Double blind cross-over design.	Pain Management Center, The University of Chicago Hospitals, Chicago, Illinois. 20 postlaminectomy patients. Mean age: 47.8, age range: 27–71, male/female: 6/14.	Epidural injections: (n = 20) 1. 8 mL (8 mg) morphine sulfate. 2. 8 mL physiologic saline at 60 min after injection of morphine or saline, 80 mg of methylprednisolone acetate was injected. Cross-over at 8 weeks, same procedure, morphine and saline were crossed.	Timing: at 0.5, 2, and 16 hours, weekly during first month, biweekly during the second month, at 6 months after injection. Outcome measures: 1. subjective pain (VAS). 2. the ability for flexion, extension, side bending, rotation of the torso (not reported). 3. the ability to resume daily activity (not reported).	Side effects: pruritus (n = 7), nausea and vomiting (n = 4), urinary retention (n = 2), bradycardia (n = 1). Score: 25.4%.	B
Garvey et al[15]	Double blind. Allocation by computer-generated four-tier entry list. Loss to follow-up: 20%.	Washington University Medical Center, Washington, DC. 63 patients with nonradiating low back pain. Mean age: 38, male/female: 41/22. duration of pain >4 weeks	Trigger-point injections: 1. 1.5 mL lidocaine 1% (n = 13). 2. 0.75 mL lidicaine 1% + 0.75 mL of Aristospan (20 mg/mL) (n = 14). 3. dry needlestick (acupuncture) (n = 20). 4. 10-second spray of ethyl chloride + 20-second acupressure (n = 16).	Timing: at 2 weeks. Outcome measures: pain on a scale of 1–10 improved *vs* not improved.	Side effects: increased pain: injection (n = 1), dry-needle stick (n = 2). Fever, chills, and systemic upset: dry needlestick (n = 1). Score: 34.8%.	A

(*Table continues*)

Table 1. Continued

Study	Methods	Participants	Interventions	Outcomes	Notes	A*
Glynn et al[16]	Randomized controlled trial. Cross-over trial. Double blind, compromised by side effects of morphine. Second intervention occurred only in failures (after first intervention), so incomplete cross-over. Statistical tests: Wilcoxon paired test.	Oxford Regional Pain Relief Unit, and Pain Relief Research Unit, Abingdon Hospital, UK. 20 patients with arachnoiditis, low back pain, or postoperative scar pain. Mean age: 52, age range: 22–76, male/female: 2/18, mean duration of pain: 6.7 months (range, 1–20).	Epidural injections: (n = 20) 1. 10 mL bupivacaine 0.5% + morphine (5 mg). 2. 10 mL bupivacaine 0.5% + clonidine (150 μg). Bupivacine on Day 1, either morphine or clonidine on Day 2, either clonidine or morphine on Day 3, providing the pain had returned.	Timing: 3 hours after injection. Outcome measures: 1. pain intensity at different point in time summed to obtain an estimate of the area under the time-effect curve, pain measured by VAS and by word score. 2. pain relief (VAS). 3. mood scores (no statistical difference; not poolable).	Side effects: morphine: pruritus (n = 12), nausea (n = 7), vomiting (n = 2); clonidine: hypotension in all patients. The result suggests that the noradrenergic system may be as important as the opoid system. Score: 40.3%.	C
Hameroff et al[18]	Randomized cross-over trial, double blind. Statistical tests: ANOVA.	University of Arizona, Health Sciences Center, Tucson, Arizona. 15 participants with myofascial pain syndrome. No further data on patient characteristics given.	Trigger point injections (n = 15). 1. 2–3 mL solution per triggerpoint consisting of 0.5% bupivacaine (150–180 mg). 2. 2–3 mL solution of 1% etidocaine (300–360 mg). 3. 2–3 mL injected at 10–18 triggerpoints during each treatment consisting of physiologic saline without preservative.	Timing: before treatment, 15 minutes, 24 hours, and 7 days after treatment. Outcome measures: 1. average pain (1 *vs* 3 $P = 0.005$; 2 *vs* 3 $p = 0.001$). 2. pain incidence (1 *vs* 3 NS; 2 *vs* 3 NS). 3. effect of pain on average physical activity (1 *vs* 3 NS; 2 *vs* 3 NS). 4. muscle tension (1 *vs* 3 NS; 2 *vs* 3 $P = 0.001$). 5. effect of pain on sleep (1 *vs* 3 NS; 2 *vs* 3 NS). 6. effect of pain on mood (1 *vs* 3 NS; 2 *vs* 3 $P = 0.026$).	No side effects. Percentage of patients with pain relief not presented by group. Significant reduction in average pain relief at 7 days after injection ($P < 0.05$). Score: 24.4%.	B
Lilius et al[22,23]	Randomized controlled trial. No information on method of randomization. Statistical tests: chi-square and *t* test, linear and logistic regression.	Helsinki University Central Hospital. 113 patients were randomized; 109 patients received injections; 106 patients were analyzed (3 did not attend for follow-up). The patients had unilateral pain without root pain with slight radiating pain to the posterior aspect of the thigh in 62 patients. History of operation for a disc lesion in 27 patients, neurologic deficit in 21 patients. Mean age: 44, age range: 19–64, 61 women and 48 men. Duration of low back pain >3 months. Mean duration: 13.4 months, range: 3–36 months.	Facet joint injections: 1. intracapsular injection of 6 mL (30 mg) bupivacaine hydrochloride (Marcaine) + 21 (80 mg) methylprednisolone into two adjoining facet joints (n = 28). 2. pericapsular injection of bupivacaine + methylprednisolone (n = 39). 3. injection of 8 mL normal saline into two facet joints (n = 42).	Timing: at 1 hour, 2 weeks, 6 weeks, and 3 months after injection. Outcome measures: 1. work outcome: returned to work (NS on short or long term). 2. subjective outcome: symptom-free, better, or slightly better (assessed by patient). 3. objective disability score at 6 weeks follow-up (good *vs* poor). 4. pain graded by VAS (NS on short or long term). 5. flexion of the spine, thoracolumbar lateral flexion and extension (no between-group comparisons). 6. rotation of the spine (no between-group comparisons).	No difference in effectiveness between intervention groups. The presentation of the data does not allow conclusions on the percentage of patients with pain relief by group. No information on comparability of baseline variables. Side effects: numbness or weakness of a limb (7/106). Percentage of patients with pain relief not presented by group Methodologic score: 25.0%.	B

(*Table continues*)

ticosteroid and saline injections 1 and 3 months after injection. The short-term risk ratio (RR) was 0.89 (95% CI = 0.65–1.21) and long-term RR was 0.90 (95% CI = 0.69–1.17). These numbers indicate that there was no significant difference between the groups. At 6 months, the percentage of patients with marked or very marked improvement was significantly higher in the group treated with methylprednisolone (46% *vs* 15%; $P = 0.002$). Despite this latter finding, it was concluded that the efficacy of facet-joint injections is small because 11 of

Table 1. Continued

Study	Methods	Participants	Interventions	Outcomes	Notes	A*
Marks et al[26]	Random number system. Concealment of assigned technique from referring clinicians and patients (double blind). Loss to follow-up: none at 1 month, 3 at 3 months.	Pain Clinic or Back Clinic, Dundee, Scotland. 86 patients with lumbar or lumbosacral pain. Excluded were patients with radicular symptoms, SLR <60, evidence of progressive spinal disorder of nondegenerative origin. Facet joint injection (n = 42): median age: 44, age range: 24–58, male/female: 20/22. Facet nerve block (n = 44): median age: 42, age range: 27–57, male/female: 26/18. Duration of pain >6 months. Median duration (range) in injection group: 10 (2–35) and in nerve block group: 7 (1–25).	1. Facet joint injection with 0.5 mL (20 mg) methylprednisolone acetate + 1.5 mL lignocaine (1%) (n = 42). 2. Facet nerve block of the medial articular branch of the posterior primary ramus from L1 to L4 (n = 44).	Timing: at 1 and 3 months after infiltration. Outcome measures: 1. change in spinal pain (1 and 2 reported combined). 2. change in referred pain.	Side effects: no serious complications. Transient symptoms, such as headache, paresthesia of one leg, nausea, and worsening of pain, occurred 15 times in the injection group and 18 times in the nerve block group. Techniques equally valid according to authors. Score: 73.5%.	A
Mathews et al[27]	Stratification by age and gender. Double blind. Survival curve analyses based on cumulative totals recovered. Use of Cox's regression. Cointerventions: consumption of paracetamol very similar in both groups.	St Thomas Hospital, London, UK. 57 patients with sciatica with a single root compression (n = 57). Experimental group: median age: 38, age range: 22–59, male/female: 19/4, median duration of pain: 4 weeks (range: 8 days–3 months). Control group: median age: 41, age range: 18–58, male/female: 24/10, median duration of pain: 4 weeks (range: 3 days–9 weeks).	Epidural injections: 1. 20 mL bupivacaine 0.125% + 2 mL (80 mg) methylprednisolone acetate (n = 23). 2. 2 mL lignocaine (over the sacral hiatus or into a tender spot) (n = 34). Frequency: at fortnightly intervals, up to three times as needed.	Timing: four times in the first 2 weeks, at 1, 3, 6, and 12 months. Outcome measures: 1. pain (recovered *vs* not recovered). 2. ranges of movement (no significant differences; data not reported). 3. SLR (no significant differences; data not reported). 4. neurologic examination (no significant differences; data not reported).	Side effects: none. Score: 66.8%.	B
Ongley et al[33]	Randomized allocation by random numbers table. Double blind (patients and observers).	Sansum Medical Clinic, Santa Barbara, California. 81 patients with chronic back pain, duration more than 1 year. Experimental: mean age (range) 45 (23–70), 18 males, years of pain (range) 8.98 (1–30), 12 patients with radiation of pain in legs. Control group: mean age (range) 43 (23–70), 20 males, years of pain (range) 10.72 (1–35), 12 patients with radiation of pain in legs.	Local injections and manipulation 1. Forceful manipulation and injection with dextrose (25%), glycerine (25%), phenol (2.5%), and pyrogen free water to 100%. This solution was diluted with 0.5% plain lignocaine hydrochloride. Injection in several sites, 60 mL in total. Infiltration of 50 mg triamcinolone dissolved in 10 mL 0.5% lignocaine into gluteus medius origin. (n = 40). 2. Light manipulation and injection with sterile 0.9% saline. Less than 10 mL at same sites. Infiltration of lignocaine into gluteus medius origin. (n = 41).	Timing: baseline, 1, 3, and 6 months after intervention Outcome measures: 1. Roland disability questionnaire added with 9 questions from Waddell's chronic disability index. 2. VAS. 3. pain diagram.	Side effects: pain and stiffness for 12–24 hours after injection, increase in menstrual flow: experimental (n = 2), control (n = 1). Postmenopausal spotting: experimental (n = 2). Headache and cough: control (n = 1). Score: 67.4%.	A
Rocco et al[41]	Randomized controlled trial. Double blind. Statistical tests: chi-square and ANOVA.	Pain Treatment Service, Brigham and Women's Hospital, Boston, Massachusetts. 24 patients. 1 lost to follow-up, 1 had a subarachnoid injection. Patients with low back pain with miscellaneous causes. Group 1: mean age: 48.9, male/female: 4/4 Group 2: mean age: 50.1, male/female: 2/5. Group 3: mean age: 52.0, male/female: 4/3.	Epidural injections: 1. 1.9 mL (75 mg) triamcinolone diacetate + 1 mL (50 mg) lidocaine (n = 8). 2. 8 mL (8 mg) morphine + 1 mL (50 mg) lidocaine (n = 7). 3. 1.9 mL (75 mg) triamcinolone diacetate + 8 mL (8 mg) morphine + 1 mL (50 mg) lidocaine (n = 7). Frequency: three times at 1 month intervals.	Timing: at 6 months after injection. Outcome measures: 1. functional impairment (by questionnaires) (not reported). 2. psychological dysfunction (not reported). 3. pain.	Side effects: marked ventilatory depression. Unethical to continue the study. Score: 47.8%.	B

(*Table continues*)

Table 1. Continued

Study	Methods	Participants	Interventions	Outcomes	Notes	A*
Rogers[42]	A randomized, single-blind, sequential analysis. Patients were admitted consecutively and randomized within blocks of two, according to the toss of a coin. The treatment was given by an investigator different from the assessor.	30 patients with a clinical diagnosis of sciatica who had neuritic pain limiting passive SLR to less than 60° from the horizontal. In steroid group: mean age (range): 42 (22–61), male/female: 7/8, mean pain duration (range): 23 (1–240) months. In nonsteroid group: mean age (range): 41 (23–63), male/female: 7/8, mean pain duration (range): 25 (1–204) months.	Epidural injections: 1. 14 mL lignocaine 2%, methylprednisolone acetate 80 mg in 2 mL aqueous suspension and 4 mL normal saline (n = 15). 2. 14 mL lignocaine 2% with 6 mL normal saline (n = 15).	Timing: at 1 month Outcome measure (sum of changes in four categories): 1. pain score. 2. work status (not poolable). 3. analgesic consumption (not poolable). 4. passive SLR: improved (+1), no change (0), worse (−1). Thus a total score of +4 to −4 was possible for each patient.	At baseline, all patients in both groups had moderate to very severe pain. At 1 month, 7/15 patients (47%) in the steroid and 3/15 patients (20%) in the nonsteroid group had no or mild pain. Side effects were not mentioned. Score: 56.4%.	B
Serrao et al[46]	Double blind (patient and observer). Statistical tests: chi-square, Fisher exact, Wilcoxon.	York Pain Clinic, Department of Anaesthetics, York District Hospital, York, UK. 28 patients included with mechanical low back pain excluded disc lesions and spinal claudication. Midazolam group: median age (range): 49 (38–70), 3 males, duration of pain (range) 4.66 years (1–35). Steroid group: median age (range) 42.5: (33–79), 6 males, duration of pain range: 8 years (1.5–24).	Epidural injections 1. 80 mg prednisolone suspended in 10 mL saline (epidural) and 3 mL (5%) dextrose solution (intrathecal) (n = 14). 2. 10 mL normal saline (epidural) and 2 mg midazolam dissolved in 3 mL (5%) dextrose (intrathecal) (n = 14).	Timing: before then 2 weeks and 2 months after injection Outcome measures: 1. Short-Form McGill Pain Questionnaire. 2. VAS. 3. verbal rating scale for sensory and affective components of pain experience (not poolable). 4. pain diary, quality of sleep. 5. self-administered analgesic medication.	Side effects: Headaches: midazolam (n = 7), steroid (n = 8). Nausea: midazolam (n = 1), steroid (n = 2). Score: 22.9%.	B
Simmons et al[47]	Randomized, double blind (patient and observer). Statistical tests: chi-square.	Alamo Bone & Joint Clinic, San Antonio, Texas. 25 patients with sciatica of longer than 6 weeks duration after failure of conservative treatment. Age 18–65 years. Exclusion of patients on systemic steroids.	Intradiscal injections: 1. methylprednisolone 80 mg/mL (n = 14). 2. bupivacaine 0.5% 1.5 mL (n = 11).	Timing: 10–14 days after discography. Outcome measures: 1. Oswestry Pain Questionnaire. 2. pain VAS. 3. pain diagram (grid scoring).	Side effects not reported.	B
Sonne et al[49]	Randomized, double blind (patient and observer) with third-party administration. Statistical tests: Fisher's exact test, Mann-Whitney *U* test. One dropout in group 1.	Department of Rheumatology, Bispebjerg Hospital, Copenhagen, Denmark. 30 patients with low back pain of longer than 1 month duration. Mean age (range) 57 (26–79) years. 8 males.	Local injections 1. 5 mL lignocaine 1% mixed with 1 mL methylprednisolone, injected at iliolumbar ligament (n = 14). 2. 5 mL isotonic saline injected at iliolumbar ligament (n = 15). A maximum of 3 injections were given at 1 week intervals.	Timing: at each visit and 2 weeks after completing the study Outcome measures: 1. pain VAS. 2. spinal flexion (no significant difference: data not shown).	1 dropout in experimental group. Side effects not reported.	B

A* = Allocation concealment where A = adequate, B = unclear, C = inadequate, and D = not used; VAS = Visual Analogue Score; ANOVA = analysis of variance; ANCOVA = analysis of covariance; SLR = straight leg raising; NS = not significant; GP = general practice; HNP = herniated nucleus pulposus.

the 22 patients in the steroid group who reported substantial improvement at 6 months after injection reported no benefit at earlier evaluations. No pharmacologic or biologic explanation can be offered for these results. Moreover, cointerventions were more frequent in the steroid group. The study of Lilius et al (1989, 1990) reported that mean scores for pain relief with methylprednisolone, bupivacaine, or both were not superior to those for placebo injections. The study by Lilius did not report proportions of patients with pain relief. The pragmatic trial of Marks et al (1992) found that facet-joint injections with methylprednisolone and lignocaine produced slightly better results than the facet nerve blocks. The response usually was short-lived: 3 months after therapy, only two patients continued to report complete pain relief. The short-term RR was 0.81 (95% CI = 0.62–1.06), and the long-term RR was 0.91 (95% CI = 0.74–1.12). These numbers indicate that no significant difference was found between the groups. The subcategories of studies on facet-joint injections (explanatory and pragmatic) contained only one study, so pooling of the data was not possible.

With respect to epidural injections, the studies by Cuckler et al (1985) and Beliveau (1971) were consid-

Table 2. Characteristics of Excluded Studies

Study	Reason for Exclusion
Dilke et al[11]	Acute complaints <1 month duration
Dreyfuss et al[12]	Diagnostic study, no RCT
Frost et al[14]	Not randomized
Gunn et al[17]	No injection therapy (only dry needling in an acupuncture-like fashion), also seriously flawed in allocation (failures 2/29 *vs* 12/27)
Klenerman et al[19]	Duration of complaints not described
Lord et al[24]	Cervical facet joint injections: falls not within the scope of this review
Lord et al[25]	Cervical facet joint injections: falls not within the scope of this review
Milligan et al[29]	Injection took place during surgery, directly in the wound
North et al[32]	Study on diagnostic and prognostic value of temporary nerve blocks using local anesthetics: falls not within the scope of this review
Porsman and Friis[35]	Acute complaints <1 month duration
Revel et al[38]	Therapeutic efficacy of facet joint blocks not evaluated in this study
Revel et al[37]	Study on discectomy *versus* chemonucleolysis; falls outside the scope of this review
Schwarzer et al[45]	Patient series, no RCT
Schwarzer et al[44]	Patient series, no RCT
Schwarzer et al[43]	Patient series, no RCT
Snoek et al[48]	Acute complaints <1 month duration
von Stratz[50]	Acute complaints <1 month duration
Wilber[52]	Not randomized
Yates[53]	Duration of complaints not described

RCT = randomized controlled trial.

ered to be explanatory studies. These studies used procaine rather than procaine combined with methylprednisolone in the control groups. Whether injection with procaine may be considered a placebo injection is not clear. No available studies compare a lignocaine or procaine injection with a saline injection. There might be some specific effects from an injection with a local anesthetic including "interruption of sustained neural activity that produced and perpetuated the pain, relaxation of paraspinal muscle spasm, and resolution of accompanying reflex sympathetic dystrophy." However, from a pharmacologic point of view, procaine is unlikely to result in lasting pain relief because it has a very short duration of action (20 to 45 minutes) (Ritchie, 1990). For this reason, treatment with procaine was considered to be placebo treatment.

Altogether, there were four explanatory trials on the short-term efficacy of epidural injections (Beliveau, 1971; Bush and Hillier, 1991; Carette et al (b), 1997; Cuckler et al, 1985). All the trials reported that pain relief within 6 months after intervention occurred more often in the experimental group, but the differences in proportions of patients with improvement were not statistically significant (alpha = 0.05; pooled RR = 0.93; 95% CI = 0.79–1.09). Three of these trials (Bush and Hillier, 1991; Carette et al (b), 1997; Cuckler et al, 1985) reported on pain relief more than 6 weeks after intervention (pooled RR = 0.92; 95% CI = 0.76–1.11). These numbers indicate that there was no significant difference between the groups.

Six pragmatic trials reported on short-term pain relief (Breivik et al, 1976; Dallas et al, 1987; Glynn et al, 1988; Mathews et al, 1987; Rocco et al, 1989; Rogers, 1992). Four of these six trials showed a nonsignificant positive effect. One study showed a significant difference between morphine–steroid and saline–steroid injections regarding pain relief within 6 weeks (Dallas et al, 1987). However, only 65% of the patients reported pain relief that lasted only 1 day to 6 weeks. Morphine was found to cause adverse side effects frequently. None of the two pragmatic trials reporting on long-term pain relief by epidural injection found significant differences between treatment groups (Mathews et al, 1987; Serrao et al, 1992).

With respect to local injections, five explanatory trials were identified (Collée et al, 1991; Garvey et al, 1989; Hameroff et al, 1981; Ongley et al, 1987; Sonne et al, 1985). Four of these studies indicated that injection therapy was more effective than placebo injection, irrespective of the medication used (Collée et al, 1911; Hameroff

Table 3. Methodologic Score

Author	Year	Methodologic Score
Carette et al	1991	83.1
Carette et al	1997	76.3
Marks et al	1992	73.5
Ongley et al	1987	67.4
Mathews et al	1987	66.8
Cuckler et al	1985	57.1
Rogers et al	1992	56.4
Breivik et al	1976	54.1
Rocco et al	1989	47.8
Collee et al	1991	47.4
Glynn et al	1988	40.3
Bush and Hillier	1991	39.9
Garvey et al	1989	34.8
Simmons et al	1992	32.2
Sonne et al	1985	28.1
Dallas et al	1987	25.4
Lilius et al	1990	25.0
Hameroff et al	1981	24.4
Beliveau	1971	23.8
Lilius et al	1989	23.0
Serrao et al	1992	22.9

Table 4. Methodologic Quality (Internal Validity Items)

Study	B	D	E	F	I	J	K
Carette et al[6]	15	7.1	12	10	2	2	2
Carette et al[5]	15	4.3	8	4	2	2	2
Marks et al[26]	15	5.7	12	10	2	—	2
Ongley et al[33]	15	5.7	12	10	2	—	2
Mathews et al[27]	15	4.3	12	10	2	—	2
Cuckler et al[8]	—	4.3	12	10	2	2	2
Rogers et al[42]	—	7.1	12	10	2	—	2
Breivik et al[3]	15	1.4	12	10	2	2	2
Rocco et al[41]	—	4.3	12	10	2	2	2
Collee et al[7]	—	2.9	12	—	2	2	2
Bush and Hillier[4]	—	1.4	12	4	2	—	2
Glynn et al[16]	—	8.6	12	—	2	—	—
Garvey et al[15]	15	—	2	—	1	—	2
Simmons et al[47]	—	1.4	12	—	2	—	2
Sonne et al[49]	—	1.4	10	—	2	2	2
Dallas et al[9]	—	8.6	—	—	2	—	—
Lilius et al[22]	—	—	—	—	2	—	2
Hameroff et al[18]	—	8.6	—	—	2	—	2
Beliveau[1]	—	—	2	10	—	—	—
Lilius et al[23]	—	—	—	—	2	—	2
Serrao et al[46]	—	1.4	2	—	2	—	2

et al, 1981; Ongley et al, 1987; Sonne et al, 1985). One study showed the opposite effect (Garvey et al, 1989): A single dry needlestick acupuncture appeared to be more effective than injections with steroid, lidocaine, or both, although the difference in effect was not statistically significant. After the results from three explanatory trials that presented raw data on the proportions of patients with short-term pain relief (Collée et al, 1991; Garvey et al, 1989; Sonne et al, 1985) were pooled, the RR was 0.80 (95% CI = 0.40–1.59). These numbers indicate that there was no significant difference between the groups. The only explanatory trial on long-term pain relief, that of Ongley et al (1987), reported a significant difference in proportions of patients with pain relief between the two groups (88% *vs* 39%; RR = 0.79; 95% CI = 0.65–0.96), indicating that local injection combined with forceful manipulation was superior to placebo injection combined with light manipulation.

There were two pragmatic trials on local injections (Mathews et al, 1987; Simmons et al, 1992). Neither of these trials showed significant differences between treatment groups.

Side Effects

In general, few side effects were reported by the studies on epidural and local injection therapy with anesthetics or steroids. The use of morphine often was associated with side effects such as pruritus, nausea, and vomiting.

■ Discussion

This systematic review of 21 clinical trials on the effectiveness of injection therapy in patients with chronic low

Table 5. Methodologic Quality (Other Items)

Study	A	C	G	H	L	M	N	O
Carette et al[6]	4	8	5	2	3	6	—	5
Carette et al[5]	4	12	5	2	5	4	2	5
Marks et al[26]	4	4	5	—	0.8	6	2	5
Ongley et al[33]	2	4	4	2	1.7	6	2	1
Mathews et al[27]	2	—	5	—	2.5	6	2	4
Cuckler et al[8]	4	4	5	—	0.8	6	—	5
Rogers et al[42]	4	—	5	—	3.3	6	—	5
Breivik et al[3]	2	—	5	—	1.7	—	—	1
Rocco et al[41]	2	—	5	—	2.5	6	—	—
Collee et al[7]	4	—	5	2	2.5	6	2	5
Bush and Hillier[4]	2	—	5	—	2.5	6	2	1
Glynn et al[16]	—	—	5	—	1.7	4	2	5
Garvey et al[15]	2	—	5	—	0.8	4	2	1
Simmons et al[47]	2	—	5	—	0.8	2	—	5
Sonne et al[49]	2	—	3	—	1.7	4	—	—
Dallas et al[9]	2	—	5	—	0.8	6	—	1
Lilius et al[22]	—	4	5	—	3	6	2	1
Hameroff et al[18]	—	—	5	—	0.8	4	2	—
Beliveau[1]	2	—	4	—	0.8	—	—	5
Lilius et al[23]	2	4	5	—	3	4	—	1
Serrao et al[46]	2	—	5	—	2.5	4	2	—

back pain shows that very little useful information can be derived from these studies. Injections into the facet joints do not seem to be effective, but with only one explanatory trial (a comparison with saline) of good quality to be found in this field (Carette et al (a), 1991), conclusions must be drawn with prudence.

No conclusion can be stated regarding the effect of epidural injection therapy. Four explanatory trials showed nonsignificant positive results from epidural injections, but the pooled odds ratio was not significantly different from 1. The short-term RR (based on four trials) was 0.93 (95% CI = 0.79–1.09). The long-term RR (based on three trials) was 0.92 (95% CI = 0.76–1.11).

These numbers indicate that there was no significant difference between the groups. With respect to local injections at trigger points or ligaments, four of five explanatory trials consistently indicated more pain relief at these locations than that offered by placebo injections. The pooled short-term RR (based on three trials) was 0.80 (95% CI = 0.40–1.59). These numbers indicate that there was no significant difference between the groups. The results on long-term pain relief were reported by only one trial (Ongley et al, 1987), which found a statistically significant difference between treatment groups (RR = 0.79 (95% CI = 0.65–0.96). These numbers indicate that trigger-point injections are better than placebo injection in terms of long-term pain relief.

Of the 21 clinical trials under review, 11 were explanatory. That is, they compared injection with active medication *versus* saline or procaine injection, which in the authors' opinion is the only way to address the question whether injection therapy is effective. The other studies compared two or more potentially active techniques to find out which was most effective. Most comparisons between different anesthetic agents did not show that one agent was significantly better than the other.

A question that remained unanswered during the review of selected trials on injection therapy is why some investigators used short-acting anesthetics such as lignocaine (Collée et al, 1991; Mathews et al, 1987) or procaine (Beliveau, 1971; Cuckler et al, 1885) instead of bupivacaine or etidocaine. The authors themselves gave no explanation for their choice.

Another issue seldom addressed involved the volume of fluid used, which, especially with epidural injections, might be important according to theoretical considerations. Volumes per epidural injection varied from 7 mL (Cuckler et al, 1985) to 42 mL (Beliveau, 1971). Evans (1930), for example, who wrote about epidural injections in the treatment of sciatica, expressed the opinion that the effect was based on the physical displacement of the neural elements caused by a large volume of injected fluid. This could lead to stretching and lysis of neural adhesions, and even to anesthesia from compressive effects. Evans (1930) observed no difference between anesthetic or physiologic saline solution in effects obtained. Whether this opinion is true or not, such considerations affect the design of the trial. If researchers believe in physical effects of injected fluid, the contrast between intervention groups should refer to the volumes injected. If they believe in pharmacologic effects, the type and duration of action from medication become more relevant.

The question whether injection therapy results in long-term pain relief was addressed by only a few studies. This is striking because the duration of pain relief is a clinically relevant issue that plays a role in the decision to use injection therapy in patients with chronic pain.

Considering methodologic quality according to standards currently recommended for conducting clinical trials, most of the reviewed studies scored low. Therefore, the opportunity for bias was high.

The current authors can think of four important reasons why potential beneficial effects from injection therapy could have been missed. First, in most of the studies, the sample sizes were too small. Therefore, the power (*i.e.*, the probability to detect small but clinically relevant differences in effect) was too low. Despite the pooled analysis, the lack of power might still be a serious problem because the studies were divided according to location of injection (facet joint *vs* epidural *vs* local), type of comparison (explanatory *vs* pragmatic), and duration of pain relief (<6 weeks *vs* >6 weeks). From the resulting 12 subcategories of studies, data from a maximum of 4 studies could be pooled.

Second, recovery rates in the groups treated by saline injections turned out to be substantial (mostly varying from 20% to 33%). There are two possible explanations for this observation: 1) Injection with saline might be effective either by a physical effect as proposed by Evans (1930) or by a placebo effect, or 2) the high recovery rates in the placebo group may reflect the natural course of low back pain, and thus, restriction of the review to trials including patients with low back pain persisting for more than 1 month did not result in the selection of study populations with low recovery rates.

Third, low back pain is not a well-specified disease entity. Many types of patients with different causes of low back pain were included. Investigators who seriously tried to select a homogeneous population had to cope with the problem that diagnosing the origin of low back pain is notoriously difficult. Such (almost inevitable) diagnostic inaccuracy results in heterogeneity of the study population, causing the effects of an intervention that might be beneficial for some types of back pain to be diluted by the inclusion of patients who cannot benefit from the intervention. For example, in an evaluation of the effect from facetal joint injections, the efficacy of the treatment method might be diluted by the inclusion of patients without a facet-joint syndrome.

Fourth, most studies measured pain on a visual analog or ordinal scale, but used dichotomized results (im-

proved *vs* not improved) in the analysis. In this way, information is unnecessarily lost, and subtle improvements that are clinically relevant could be missed.

■ Conclusions

Implications for Practice

Facet-joint, epidural, and local injection therapies have not yet been proved effective, nor have they been proved ineffective. Because of the tendency toward positive results favoring injection therapy, and because of the minor side effects reported in the reviewed studies, there currently is no justification for abandoning injection therapy for patients with low back pain. However, because statistically significant results are lacking and well-designed trials are scarce, a solid foundation for the effectiveness of injection therapy also is lacking.

Implications for Research

Facet-Joint Injections. A solid foundation for the effectiveness of injection therapy is lacking. Only one well-designed study on facet-joint injection therapy was found, and its results were statistically nonsignificant.

Epidural Injections. There is insufficient evidence for the effectiveness of epidural injection therapy. There was a tendency towards results favoring active injections over placebo injections, but the pooled relative risks were statistically nonsignificant and there was only one well designed study.

Local Injections. There is insufficient evidence to prove the effectiveness of local injection therapy. Two of three studies on the short-term effect yielded results favoring local injections over placebo injections, but the pooled relative risk was statistically nonsignificant. Only one well-designed study on the long-term effect was found that had statistically significant results favoring local injection over placebo injection.

Evidence on the effectiveness of injection therapy is still lacking. Therefore, large, well-designed trials on the effects of facet-joint, epidural, and local injection therapies are needed.

1. These trials should be explanatory because the first goal should be to compare the injection of an anesthetic, steroid, or both with placebo injection.

2. Pending proven effectiveness of injection therapy, there is less need for comparing different medications with each other.

3. Future trials should take into account important criteria for methodologic quality such as baseline comparability of groups, concealment of randomization, intention-to-treat analysis, the presentation of frequencies of the most important outcomes, and adequate sample size.

4. The clinically relevant issue of the duration of the effect on pain should receive more attention. Contrary to most trials published in this field, the focus should be on long-term pain relief instead of short-term effects.

■ Key Points

- This review included 21 randomized trials on injection therapy.
- Only 11 trials compared injection therapy with placebo injections.
- There is insufficient evidence on the effectiveness of facet joint, epidural, and local injection therapy.
- Statistically significant results are lacking, and well-designed trials are scarce.

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