

Review

Epidural Steroids in the Management of Chronic Spinal Pain: A Systematic Review

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Background: Epidural injection of corticosteroids is one of the most commonly used interventions in managing chronic spinal pain. However, there has been a lack of well-designed randomized, controlled studies to determine the effectiveness of epidural injections. Consequently, debate continues as to the value of epidural steroid injections in managing spinal pain.

Objective: To evaluate the effect of various types of epidural steroid injections (interlaminar, transforaminal, and caudal), in managing various types of chronic spinal pain (axial and radicular) in the neck and low back regions.

Study Design: A systematic review utilizing the criteria established by the Agency for Healthcare Research and Quality (AHRQ) for evaluation of randomized and non-randomized trials, and criteria of Cochrane Musculoskeletal Review Group for randomized trials were used.

Methods: Data sources included relevant English literature performed by a librarian experienced in Evidence Based Medicine (EBM), as well as manual searches of bibliographies of known primary and review articles and abstracts from scientific meetings within the last 2 years. Three reviewers independently assessed the trials for the quality of their methods. Subgroup analyses were performed among trials with different control groups, with different techniques of epidural injections (interlaminar, transforaminal, and caudal), with different injection sites (cervical/thoracic, lumbar/sacral), and with timing of outcome measurement (short- and long-term).

Outcome Measures: The primary outcome measure is pain relief. Other outcome measures were functional improvement, improvement of psychological status, and return to work. Short-term improvement is defined as 6 weeks or less, and long-term relief is defined as 6 weeks or longer.

Results: In managing lumbar radicular pain with interlaminar lumbar epidural steroid injections, the evidence is strong for short-term relief and limited for long-term relief. In managing cervical radiculopathy with cervical interlaminar epidural steroid injections, the evidence is moderate. The evidence for lumbar transforaminal epidural steroid injections in managing lumbar radicular pain is strong for short-term and moderate for long-term relief. The evidence for cervical transforaminal epidural steroid injections in managing cervical nerve root pain is moderate. The evidence is moderate in managing lumbar radicular pain in post lumbar laminectomy syndrome. The evidence for caudal epidural steroid injections is strong for short-term relief and moderate for long-term relief, in managing chronic pain of lumbar radiculopathy and postlumbar laminectomy syndrome.

Conclusion: There is moderate evidence for interlaminar epidurals in the cervical spine and limited evidence in the lumbar spine for long-term relief. The evidence for cervical and lumbar transforaminal epidural steroid injections is moderate for long-term improvement in managing nerve root pain. The evidence for caudal epidural steroid injections is moderate for long-term relief in managing nerve root pain and chronic low back pain.

Key words: Spinal pain, low back pain, cervicgia, epidural steroids, interlaminar, caudal, transforaminal, radiculopathy, axial pain, postlaminectomy syndrome, failed back surgery syndrome.

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Epidural injections for managing chronic pain are one of the most commonly performed interventions in the United States (1,2). Utilization statistics in the Medicare population of epidural procedures showed an increase from 802,735 in 1998 to 1,776,153 in 2005, or 121% over a period of 7 years. The projected statistics in the total U.S. population is expected to be 4 times the procedures performed in the Medicare population. Multiple systematic reviews (3-14), a meta-analysis (15), multiple guidelines (16-19), health technology assessments by insurers, and local medical review policies and coverage decisions have been published. However, controversy continues regarding the effectiveness of epidural steroid injections. They have been used to treat radicular pain from herniated discs, spinal stenosis, and chemical discs and axial spinal pain. The evidence is highly variable based on the reviewer and the evidence has been rated from indeterminate to strong in various publications. In addition, 3 types of epidurals, namely interlaminar, transforaminal, and caudal; and administration in 3 separate regions namely lumbar, cervical, and thoracic, with variable results complicate the picture of practice of interventional pain management.

Spinal pain is the most common of all chronic pain disorders. The lifetime prevalence of spinal pain has been reported as 54% to 80% (20-32). Annual prevalence of chronic low back pain ranges from 15% to 45% (22,23,25,30). Studies of the prevalence of low back pain and neck pain (23,25) and impact on general health showed 25% of patients reporting Grade II to Grade IV low back pain (high pain intensity with disability), whereas it was 14% in patients with neck pain. Modern evidence has shown that chronic persistent low back pain and neck pain in children, adults, and elderly are seen in up to 25% to 60% of patients, one year or longer after the initial episode (33-47). In addition, spinal pain is also associated with enormous economic, societal, and health impact (48-65). There are not any interventions which provide definite and long-term improvement in chronic low back pain, neither conservative nor surgical (66-76). Further, post-laminectomy syndrome and other symptoms, such as postsurgery syndrome, representing a cluster of syndromes wherein the expectations of the patient and the spine surgeon are not met, following spine surgery are common phenomena with persistent pain following spine surgery (77-83).

Nevertheless, the benefit and most effective route of administration for epidural steroids remain

controversial. Several approaches are available to access the lumbar epidural space; namely, interlaminar, transforaminal, and caudal (3,4,16-19,84,85). There are substantial differences among these 3 approaches. The interlaminar entry can be directed more closely to the assumed site of pathology, requiring less volume than the caudal route. The transforaminal approach is target-specific and requires the smallest volume to reach the primary site of pathology; specifically, the anterior-lateral epidural space as well as the dorsal root ganglion. On the other hand, the caudal entry is relatively easily achieved with minimal risk of inadvertent dural puncture, but requires a relatively high volume (10-20 mL) of injectate to reach the site of pathology.

The underlying mechanism of action of epidurally administered steroid and local anesthetic injections is still not well understood. It is believed that the achieved neural blockade alters or interrupts nociceptive input, reflex mechanisms of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities. Further, it is believed that local anesthetics interrupt the pain-spasm cycle and reverberating nociceptor transmission. On the other hand, corticosteroids reduce inflammation by inhibiting either the synthesis or release of a number of pro-inflammatory mediators and by causing a reversible local anesthetic effect (86-94).

The purpose of this review is to evaluate and update the effects of various types of epidural injections (interlaminar, transforaminal, and caudal) in the management of various types of chronic spinal pain (axial and radicular, cervical and lumbar). Several important studies and complications have been reported since the previous systematic review (3).

METHODS

Literature Search

The literature search included using a professional librarian from an academic medical center (Vanderbilt University Medical School, Nashville, TN) utilizing PubMed, EMBASE, and ISI Web of Science (January 1966–October 2006); systematic reviews; narrative reviews; cross-references to the reviews; various published trials; and peer-reviewed abstracts from scientific meetings during the past 2 years, published in the English language. The search strategy including the MeSH terms was performed by the librarian. Results from all 3 databases were combined and duplicates were removed. PubMed strategies included a keyword search of non-

Medline citations to retrieve in-process and supplied by publisher citations. All articles were reviewed by at least 3 authors in the group and results were scored as a mean of the 3 scores rounded up to a whole number. Table 1 in the Systematic Review of Diagnostic Utility of Selective Nerve Root Blocks in this issue of the journal illustrates search strategies utilized.

Selection Criteria

The review focused on randomized and non-randomized evaluations, and reports of complications. The population of interest was patients suffering with chronic spinal pain for at least 3 months. Three techniques of epidural injections (interlaminar, transforaminal, and caudal) with local anesthetic, steroid, or other drugs provided for management of spinal pain were evaluated. All the studies providing appropriate management with outcome evaluations of 3 months or longer and statistical evaluations were reviewed. The primary outcome measure was pain relief at various points in time. The secondary outcome measures were functional or psychological improvement, return to work, and complications.

For evaluating the quality of individual articles, we have used the criteria from the Agency for Healthcare Research and Quality (AHRQ) publication (95). For evaluation of randomized trials, criteria described

by Cochrane Review Group for musculoskeletal disorders (96) also have been utilized.

For studies to be included, an algorithmic criterion should have been met and a study should have answered positive questions (at least partially) in all 3 categories (3,4,18,19,97,98). If a study had 10 or more randomized trials meeting inclusion criteria, no observational studies were included. AHRQ criteria, Cochrane Review Group criteria, and algorithmic criteria of inclusion and exclusion are shown in multiple publications (3,4,18,19,95-98) and also in this issue of the journal in the systematic review of percutaneous adhesiolysis.

Analysis of Evidence

Qualitative analysis was conducted, using 5 levels of evidence for effectiveness of epidural steroids as illustrated in Table 1. Pain relief was evaluated on both a short-term (< 6 weeks) and long-term (6 weeks or longer) basis. A study was judged to be positive if the authors concluded that the epidural steroid injection therapy was more effective than the reference treatment in randomized trials or simply concluded that it was effective. All other conclusions were considered negative. If, in the opinion of reviewers, there was conflict with the conclusion, the conclusions were changed with appropriate explanations.

Table 1. Designation of levels of evidence.

Level I	Conclusive: Research-based evidence with multiple relevant and high-quality scientific studies or consistent reviews of meta-analyses.
Level II	Strong: Research-based evidence from at least 1 properly designed randomized, controlled trial; or research-based evidence from multiple properly designed studies of smaller size; or multiple low quality trials.
Level III	Moderate: a) Evidence obtained from well-designed pseudorandomized controlled trials (alternate allocation or some other method); b) Evidence obtained from comparative studies with concurrent controls and allocation not randomized (cohort studies, case-controlled studies, or interrupted time series with a control group); c) Evidence obtained from comparative studies with historical control, 2 or more single-arm studies, or interrupted time series without a parallel control group.
Level IV	Limited: Evidence from well-designed, nonexperimental studies from more than 1 center or research group; or conflicting evidence with inconsistent findings in multiple trials.
Level V	Indeterminate: Opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committees.

Adapted from ref 3, 16, 17, 95, 97, 98.

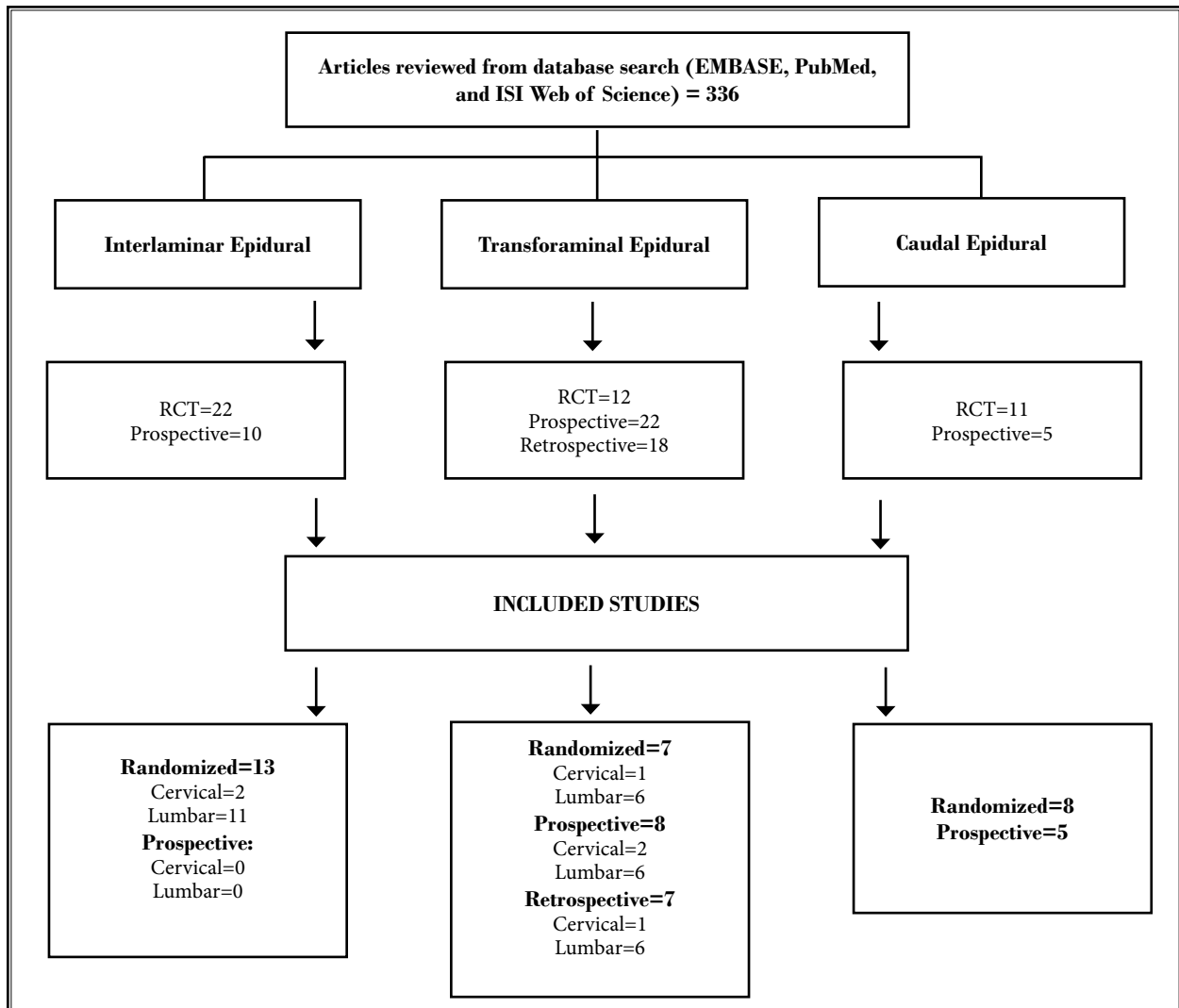


Fig. 1. Systematic review flow chart.

RESULTS

The literature search was carried out as described in the methods section. Fig. 1 shows a systematic review flow chart with number of total articles reviewed and included in each category of interlaminar, transforaminal, and caudal epidurals with itemization into randomized, prospective, and retrospective.

Interlaminar Epidural Injections

Our search strategy yielded multiple studies evaluating the effectiveness of interlaminar epidural injections. These included 22 randomized or double-blind trials (99-120), 9 non-randomized prospective trials (121-129), and multiple other observational trials (130-161).

Methodological Criteria

Of the 22 randomized trials, 13 studies met inclusion criteria (99-103,107-109,113,116,117,119,120). One study (104) was excluded as they studied effects of subarachnoid and epidural midazolam. Two studies (110,111) focused on diabetic polyneuropathy and intractable postherpetic neuralgia. One study (114) evaluated only inpatients, whereas 4 evaluations (105,106,115,118) failed to evaluate long-term relief. One study (112) was not included due to lack of data for review. Tables 2 and 3 illustrate various characteristics and results of published randomized trials meeting inclusion criteria. Eleven lumbar trials (99,100-103, 107,108,116,117,119,120) and 2 cervical trials (109,113) were included.

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Table 2. Characteristics of published randomized trials of lumbar interlaminar epidural injections.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Wilson-McDonald et al (119) Randomized, controlled trial AHRQ score: 10/10 Cochrane score: 7/10	93 pts with MRI evidence of a disc prolapse, spinal stenosis, or a combination. Pts had lumbosacral nerve root pain which had not resolved within 6 wks minimum .	Experimental: epidural injection of bupivacaine 0.5% (40 mg) with methylprednisone 80 mg. Control: intramuscular injection of 0.5% (40 mg) bupivacaine with 80 mg methylprednisone.	Timing: 6 wks, 24 mos. Outcome measures: Oswestry Disability index, pain relief.	In the first 5 wks after epidural injection a useful improvement in nerve root symptoms was seen.	Positive short-term and negative long-term relief
Arden et al (120) Double-blind, randomized placebo controlled: TRIM AHRQ score: 10/10 Cochrane score: 9/10	228 pts with unilateral sciatica .	Experimental: triamcinolone 80 mg and 10 ml of 0.25% bupivacaine Control: interspinous injection with 2 mL of normal saline.	Timing: 3, 6, 12, 26, and 52 weeks. Outcome measures: Oswestry disability index, Likert scale, SF-36, VAS.	Lumbar epidural steroid injection produced a statistically significant improvement in function over placebo in 3 wks. By 6 wks, benefit lost.	Positive short-term and negative long-term relief
Carette et al (100) Randomized, double-blind trial AHRQ score: 10/10 Cochrane score: 10/10	158 pts with sciatica due to a herniated nucleus pulposus. Treatment group: 78 Placebo group: 80.	Experimental: methylprednisolone acetate (80 mg and 8 mL of isotonic saline) Control: isotonic saline 1 mL Frequency: 3 epidural injections 3 wks apart.	Timing: 6 wks, 3 mos, 12 mos Outcome measures: need for surgery Oswestry Disability scores.	Significant improvement was seen in leg pain in the methylprednisolone group after 6 weeks, with no difference after 3 and 12 mos.	Positive short-term and negative long-term relief
McGregor et al (99) Randomized, controlled trial AHRQ score: 6/10 Cochrane score: 5/10	44 pts with low back and leg pain.	Caudal epidural vs lumbar epidural.	Visual analog scale.	No significant improvement.	Negative short-term and long-term relief
Pirbudak et al (117) Randomized non-blinded trial AHRQ score: 7/9 Cochrane score: 6/10	92 pts with sciatica. Experimental with steroids and amitriptyline: 46. Control with benzylprednisolone and bupivacaine steroids: 46.	Experimental: benzylprednisolone (14 mg) + bupivacaine and 10-50 mg oral amitriptyline.	Timing: 2 wks, 6 wks, and 9 mos. Outcome measures: VAS and Oswestry low back pain disability questionnaire.	Lumbar epidural steroid injection reported pain relief up to 6 mos. Additional oral amitriptyline increased pain relief to 9 mos.	Positive short-term and long-term relief
Snoek et al (101) Randomized trial AHRQ score: 7/10 Cochrane score: 6/10	51 pts with lumbar root compression documented by neurological deficit and a concordant abnormality noted on myelography. Experimental: 27 Control: 24.	Experimental: 80 mg of methylprednisolone (2 mL). Control: 2 mL of normal saline Frequency: single injection.	Timing: 3 days and an average of 14 mos. Outcome measures: Pain, sciatic nerve stretch tolerance.	No statistically significant differences were noted in either group.	Negative short-term and long-term relief
Cuckler et al (102) Randomized, double-blind trial AHRQ score: 9/10 Cochrane score: 9/10	73 pts with back pain due to either acute herniated nucleus pulposus or spinal stenosis of > 6 mos. Experimental: 42 Control: 31	Experimental: 80 mg (2 mL) of methylprednisolone + 5 mL of procaine 1%. Control group: 2 mL saline + 5 mL of procaine 1%.	Timing: 24 hrs and an average of 20 mos. Outcome measures: subjective improvement, need for surgery.	There was no significant short-term or long-term improvements between both groups.	Negative short-term and long-term relief

Table 2. Continued. *Characteristics of published randomized trials of lumbar interlaminar epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Dilke et al (103) Randomized trial AHRQ score: 7/10 Cochrane score: 7/10	100 pts with low back pain and sciatica of 1 week to more than 2 yrs. Experimental: 51 Control: 48.	Experimental group: 10 mL of saline + 80 mg of methylprednisolone. Control group: 1 mL of saline.	Timing: 2 wks and 3 mos. Outcome measures: pain relief, analgesic use, and resuming work.	Initial Improvement: 60% in the treatment group and 31% in the control group. A greater proportion of actively treated pts improved at 3 mos.	Positive short-term and long-term relief
Ridley et al (107) Randomized trial AHRQ score: 9/10 Cochrane score: 8/10	35 pts with low back pain and sciatica of mean duration approximately 8 mos. Experimental: 19 Control: 16.	Experimental: 10 mL of saline + 80 mg of methylprednisolone (n=19). Control: saline 2 mL, interspinous ligament (n=16).	Timing: 1 wk, 2 wks, 3 mos, and 6 mos. Outcome measures: pain control improvement in straight leg raising.	90% of the pts in the treated group compared to 19% in the control group showed improvement at 1 wk, 2 wks, and 12 wks. By 24 wks, relief deteriorated to pretreatment levels.	Positive short-term and negative long-term relief
Rogers et al (108) Randomized, single-blind, sequential analysis AHRQ score: 6/10 Cochrane score: 5/10	30 pts with low back pain. Experimental = 15 Control = 15.	Experimental: local anesthetic + steroid. Control: local anesthetic alone.	Timing: 1 month. Outcome measures: pain relief and nerve root tension signs.	Experimental group had significantly better results. Long-term results were similar for both.	Positive short-term relief and negative long-term relief
Kraemer et al (116) Randomized trial AHRQ score: 6/10 Cochrane score: 5/10	Control: 46 Intervention: 40.	Control: paravertebral local injection of local anesthetic, with intramuscular steroid injection. Intervention: lumbar interlaminar steroid injection.	Timing: 3 wks and 3 mos. Outcome measures: pain relief.	Epidural injections were more effective than paravertebral injections.	Positive short-term and negative long-term relief

Since there were multiple randomized trials evaluating lumbar pain (N=1), no prospective or retrospective evaluations were considered for inclusion. The single prospective evaluation of the cervical spine (121) was not included as all the patients who underwent interlaminar epidural steroid injections also underwent transforaminal epidural steroid injections.

Effectiveness

Of the 11 randomized trials (99,100-103,107,108,116,117,119,120) included in the evaluation of lumbar radiculitis, 7 were positive for short-term relief (100,103,107,108,116,117,119), whereas only 2 studies were positive for long-term relief (103,117).

In the evaluation of cervical pain and radiculopathy, 2 randomized trials (109,113) were

available. Both the randomized trials (109,113) evaluating the effectiveness of interlaminar cervical epidural steroids in managing cervical radiculopathy were positive.

Of the 4 randomized trials, which were positive, Dilke et al (103) studied low back pain and sciatica, and Pirbudak (117) evaluated all patients with sciatica, whereas Castagnera et al (109) and Stav et al (113) studied chronic cervical radicular pain.

Among the studies reporting negative short-term and long-term results, patients with disc herniation, spinal stenosis, and postlumbar laminectomy syndrome with low back and/or sciatica were included.

Description of Study Characteristics

Descriptive characteristics of various studies in-

Table 3. Characteristics of published randomized trials of cervical interlaminar epidural injections.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Castagnera et al (109) Randomized trial AHRQ score: 7/10 Cochrane score: 6/10	14 patients: local anesthetic and steroid. 10 patients: local anesthetic, steroid + morphine sulfate.	I. 0.5% lidocaine + triamcinolone acetonide. II. Local anesthetic + steroid + 2.5 mg of morphine sulfate.	Timing: 1 month, 3 mos, and 12 mos. Outcome measures: pain relief.	The success rate was 79% vs. 80% in group I and II. Overall, initial success rate was 96%, 75% at 1 month, 79% at 3 mos, 6 mos, and 12 mos.	Positive short-term and long-term relief
Stav et al (113) Randomized trial AHRQ score: 6/10 Cochrane score: 5/10	Experimental: 25 patients. Control: 17 patients.	Experimental: epidural steroid and lidocaine injections Control: steroid and lidocaine injections into the posterior neck muscles	Timing: 1 week and 1 year. Outcome measures: pain relief, change in range of motion, reduction of daily dose of analgesics, return to work.	One week improvement 36% vs 76%; One year improvement 12% vs 68%.	Positive short-term and long-term relief

cluded in the evidence synthesis is illustrated in Table 2 for lumbar interlaminar epidural injections and Table 3 for cervical interlaminar epidural injections.

Two new interlaminar lumbar epidural steroid injections (119,120) were included in lumbar interlaminar epidural evidence synthesis are described here.

Arden et al (120) evaluated 228 patients with "clinical" unilateral sciatica who were treated with either a lumbar epidural injection (80 mg triamcinolone in 10 mL 0.25% bupivacaine) or an interspinous ligament injection with 2 mL normal saline, performed blindly by "experienced anaesthetists." The patients underwent injections at 0, 3, and 6 weeks, although patients who noted at least 75% improvement in pain did not receive a second or third injection. The epidural injections produced a significant improvement in self-reported function at 3 weeks, but that benefit was lost by 6 weeks.

Wilson-MacDonald et al (119) compared lumbar epidural steroid injections to interspinous ligament steroid injections, to assess whether the epidural location of the steroid was responsible for the subsequent effects. Ninety-three patients with back and leg pain and MRI evidence of a prolapsed disc who had been offered surgery were randomized to receive either a blind lumbar epidural (44 patients) or an injection into the interspinous ligament (48 patients). Each patient was injected with 8

mL 0.5% bupivacaine and 80 mg of methylprednisolone. There was no difference in the rate of subsequent surgery through the period of follow up.

Cost Effectiveness

In the evaluation of cost effectiveness, Manchikanti et al (85) and Price et al (160) concluded that lumbar interlaminar epidural steroid injections were not cost effective.

Level of Evidence

In managing lumbar radicular pain with interlaminar lumbar epidural steroid injections, the level of evidence is strong for short-term relief and limited for long-term relief. In managing cervical radiculopathy with cervical interlaminar epidural steroid injections, the evidence was moderate for short-term improvement and long-term improvement. The evidence is indeterminate in the management of axial neck pain, axial low back pain, and lumbar spinal stenosis.

Transforaminal Epidural Injections

Relevant reports evaluating the effectiveness of transforaminal epidural injections included 12 randomized trials, 20 prospective evaluations, and multiple retrospective reports (121,122,130,161-212).

Methodological Criteria

The evaluation for evidence synthesis led to identification of 12 randomized controlled trials (116,162-

172), and 20 prospective evaluations (121,122,173-190), and multiple retrospective evaluations (130,161,191-206). Of the 12 randomized controlled trials, 7 trials were included in evidence synthesis (162-164,166,167,169,170), whereas of 20 prospective evaluations, 7 were included (121,174,175,187-190). Karppinen et al (166) reported results of 1 study in 2 publications (165,166). Thus, this was considered as one study. Multiple others were excluded for various reasons. A trial by Kolsi et al (168) was not included since the measurements were only of short-term duration. Kraemer et al (116) described lumbar epidural perineural injection, however, using an interlaminar approach, a non-validated technique. A summary of reported studies is listed in Table 4.

Among the 7 randomized trials included in the evidence synthesis meeting inclusion criteria, 6 of them evaluated effectiveness in lumbar disc herniation and radiculopathy (162-164,166,169,170), showing mixed

results in 4 of the 6, both in short-term and long-term with 2 negative studies (163,166). The 7th trial (167) studied effectiveness in postsurgery syndrome with negative results.

Among the 7 prospective evaluations included for evaluation, 2 studies evaluated the effectiveness of cervical transforaminal epidurals (121,189), showing positive results. The remaining 5 studies (175,179,187,188,190) evaluated lumbar transforaminal epidural steroid injections. One study (188) compared effectiveness of transforaminal epidural steroid injections in lumbar spine with discectomy. One evaluation reported the effect on spinal stenosis (190). Multiple retrospective evaluations also showed positive results. Only one retrospective evaluation (130) was included in cervical transforaminal evidence synthesis. A summary of lumbar epidural transforaminal injections is described in Table 5, whereas, the summary of cervical transforaminal epidural injections is described in Table 6.

Table 4. Details of randomized trials studying the effectiveness of lumbar transforaminal epidural steroid injections.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Riew et al (162,164) Prospective, randomized, controlled, double-blind study AHRQ score: 8/10 Cochrane score: 7/10	55 pts with lumbar disc herniations or spinal stenosis referred for surgical evaluation. 28 pts in experimental group (bupivacaine and betamethasone) and 27 pts in control group (bupivacaine only).	Experimental: transforaminal nerve root or epidural steroid injection with 1 mL of 0.25% bupivacaine and 6 mg of betamethasone Control: 1 mL of 0.25% bupivacaine. As many as 4 injections were given during the follow-up.	Initial outcomes were evaluated at 1 year. Injection was considered as a failure if the patient opted for operative treatment. North American Spine Society questionnaire also used: 20 of 28 patients in steroid group, 9 of 27 patients in control group had no surgery at 1 year. After 5 yrs, with no differences among groups.	17 of the 21 pts still had successful results with no operative intervention.	Positive short-term and long-term relief
Ng et al (163) Randomized, double-blind, controlled trial AHRQ score: 8/10 Cochrane score: 8/10	43 pts were recruited in the bupivacaine and methylprednisolone group and 43 pts in the bupivacaine only group with radicular pain who had unilateral symptoms and also failed conservative management.	One group received bupivacaine and methylprednisolone and the second group received only bupivacaine with a transforaminal injection.	Outcome measures: the Oswestry Disability Index, visual analogue score for back pain and leg pain, claudication in walking distance, and the patient's subjective level of satisfaction of the outcome.	47.5% of pts in the bupivacaine only group had at least 20 mm reduction in leg pain compared to 41.5% of pts in the bupivacaine and steroids group at 3 months.	Negative short-term and long-term relief

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Table 4 Continued. *Details of randomized trials studying the effectiveness of lumbar transforaminal epidural steroid injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Karppinen et al (165, 166) Randomized, double-blind trial AHRQ score: 9/10 Cochrane score: 8/10	160 consecutive, eligible pts with sciatica with unilateral symptoms of 1 to 6 mos duration. None of the pts had undergone surgery.	Experimental: local anesthetic and methylprednisolone. Control: normal saline.	Timing: 2 wks, 3 mos, and 6 mos Outcome measures: Pain relief, sick leave, medical costs, and future surgery. Nottingham Health Profile.	Steroid injection produced significant treatment effects and short-term in leg pain, straight leg raising, disability and in Nottingham Health Profile and emotional reactions.	Positive short-term and long-term relief
Vad et al (169) Prospective, randomized trials AHRQ score: 7/10 Cochrane score: 7/10	Pts with leg pain, with documented herniated nucleus pulposus or manifested clinical signs such as radicular pain with lumbar radiculopathy.	Experimental: betamethasone 9 mg, and 2% preservative-free Xylocaine (1.5 mL) per level. Control: trigger point injections.	Timing: 3 wks, 6 wks, 3 mos, 6 mos, and 12 mos. Outcome measures: Roland-Morris score, visual numeric score, finger-to-floor distance, patient satisfaction score.	Group receiving transforaminal epidural steroid injections had 84% success rate compared with 48% for group receiving trigger point injections.	Positive short-term and long-term relief
Devulder (167) Open, non-blind, randomized study AHRQ Score: 6/10 Cochrane Score: 5/10.	60 pts with documented epidural fibrosis in fewer than three nerve roots.	Group A = 1 mL bupivacaine 0.5% with 1500 units hyaluronidase and 1 ml saline per nerve root sleeve. Group B = 1 mL bupivacaine 0.5% with 40 mg methylprednisolone solution per nerve root. Group C = bupivacaine 0.5% combined with 1500 units hyaluronidase and 40 mg methylprednisolone solution. The volume of each injection was 2 ml and each was given twice at an interval of 1 wk.	The pts were evaluated on a verbal pain rating scale 1, 3, and 6 mos after the second injection. The Kruskal-Wallis test was used to detect statistically significant differences among the three groups, and the analysis was refined with the Friedman test.	Overall, although injections induced analgesia at 1 month, these effects were reduced at 3- and 6-month follow-ups. No statistical differences were found between the 3 treatment groups after 1 month.	Negative short-term and long-term relief
Thomas (170) Randomized, controlled trials AHRQ Score: 6/10 Cochrane Score: 5/10	Thirty-one pts (18 females, 13 males) with discal radicular pain of less than 3 mos duration.	Pts were consecutively randomized to receive either radio-guided transforaminal or blindly performed interspinous epidural corticosteroid injections.	Post-treatment outcome was evaluated clinically at 6 and 30 days, and 6 mos. Outcome measures: pain, functional status.	At day 30 and 6 mos, pain relief, daily activities, work, leisure activities, anxiety, and depression, were better in transforaminal group.	Positive short-term and long-term relief

Table 5. Details and results of nonrandomized trials of lumbar transforaminal epidural injections.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Lutz et al (179) A prospective case series AHRQ score: 4/8	69 pts with lumbar herniated nucleus pulposus and radiculopathy were recruited.	Transforaminal epidural steroid injections with 1.5 cc of 2% Xylocaine and 9 mg of betamethasone acetate.	Timing: 28 to 144 wks. Outcome measures: At least \pm 50% reduction in preinjection and postinjection visual numerical pain scores.	A successful outcome was reported by 52 of the 69 pts (75.4%) at an average follow-up of 80 wks (range 28-144 wks).	Positive short-term and long-term relief
Butterman (187) A prospective evaluation AHRQ score: 4/8	232 pts who were referred for treatment of DDD, 171 pts who were possible spinal arthrodesis candidates.	Transforaminal epidural steroid injections or intradiscal steroid injections (ISIs).	Visual analog pain scale, pain drawing, Oswestry Disability Index, use of pain medication, and opinion of treatment success.	ESI was effective in improving pain and function at short-term follow-up. At 2 years, less than one-third had not had additional invasive treatment.	Positive short-term and negative long-term relief
Butterman (188) A prospective evaluation AHRQ score: 4/8	169 pts with a large herniation of the lumbar nucleus pulposus.	Transforaminal epidural steroid injection or discectomy.	Evaluation was performed with the use of outcomes scales and neurological examination.	42% to 56% of the 50 pts who had epidural steroid injection reported that the treatment had been effective.	Positive short-term and long-term relief
Botwin et al (190) A prospective evaluation AHRQ score: 4/8	34 pts who met our inclusion criteria for the treatment of unilateral radicular pain from degenerative lumbar spinal stenosis.	Injectant: 12 mg of betamethasone acetate and 2 mL of 1% preservative-free lidocaine HCL.	Pts were evaluated by an independent observer at 2 mos, and at 12 mos after the injections. Questionnaires: visual analog scale, Roland 5-point pain scale, standing/walking tolerance, and patient satisfaction scale.	75% of pts had successful long-term outcome, reporting at least a >50% reduction between preinjection and postinjection pain scores, with an average of 1.9 injections per patient. 64% of pts had improved walking tolerance, and 57% had improved standing tolerance at 12 mos.	Positive short-term and long-term relief
Yang et al (175) A prospective evaluation AHRQ score: 4/8	21 patients with lumbar radiculopathy were evaluated. All of them had a CT or MRI visualized disc herniations and were felt to be candidates for discectomy.	Transforaminal epidural steroid injection.	Pain relief and avoidance of surgery.	63% of patients had significant pain relief lasting through the 23-month follow-up, avoiding surgery.	Positive short-term and long-term relief

Description of Study Characteristics

Riew et al (162) performed an evaluation of minimum 5-year follow-up to evaluate nerve root blocks in the treatment of lumbar radicular pain. This was a continuation of a previous randomized, double-blind, controlled study on the effect of nerve root blocks on the need for operative treatment of lumbar radicular

pain (164). All of the patients in both studies (162,164) were considered to be operative candidates by the treating surgeon and all had initially requested operative intervention. They had then been randomized to be treated with a selective nerve root block with either bupivacaine or bupivacaine and betamethasone. Both the treating physician and the patient were

Table 6. Details and results of non-randomized trials of cervical transforaminal epidural injections.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Bush and Hillier (121) A prospective evaluation AHRQ score: 4/8	68 pts with neck pain and cervical radiculopathy.	Transforaminal cervical epidural steroid injections.	Timing: 1 month to 1 year. Outcome measures: Pain relief.	93% of the pts were reported to have good pain relief lasting for 7 mos.	Positive short-term and long-term relief.
Cyteval et al (189) AHRQ score: 4/8	30 pts with cervical radiculopathy, 16 pts with foraminal degenerative stenosis, 14 pts with disk herniation.	Periradicular foraminal steroid infiltration under CT control.	Timing: 2 wks, 6 mos. Outcome measures: visual analog pain scale (VAS).	Good pain relief was reported in 60% of pts. There was no rebound of pain at the 6-month follow-up.	Positive short-term and long-term relief
Kolstad et al (174) A prospective evaluation AHRQ score: 4/8	21 patients awaiting cervical disc surgery.	Patients were given 2 epidural injections 2 weeks apart.	Outcome assessments: 6 weeks and 4 mos . Outcome measures: VAS, Odom's criterion, and treatment satisfaction.	5 of the 21 patients canceled their surgery due to improvement in pain, and overall, there was a significant decrease in radicular pain at 6 weeks and 4 months.	Positive short-term and long-term relief
Lin et al (130) A retrospective study AHRQ score: 4/8	Patients with herniated cervical discs, otherwise surgical candidates were offered a trial of cervical epidural injections.	Cervical transforaminal with local anesthetic and steroids.	Pain relief and avoidance of surgery.	Of the 70 treated patients, 44 (63%) had significant relief of their symptoms and did not wish to proceed with surgical treatment.	Positive short-term and long-term relief

blinded to the type of medication. Of the 55 randomized patients, 29 avoided an operation in the original study. Twenty-one of those 29 patients were reevaluated with a follow-up questionnaire at a minimum of 5 years after the initial block; 17 of 21 patients still had not had operative intervention. There was no difference between the group treated with bupivacaine alone and the group treated with bupivacaine and betamethasone with regard to the avoidance of surgery for 5 years. At the 5-year follow-up evaluation, all of the patients who had avoided operative treatment had significant decreases in neurological symptoms and back pain compared with baseline values. Authors concluded that the majority of patients with lumbar radicular pain who avoid an operation for at least 1 year after receiving a nerve root injection with bupivacaine along or in combination with betamethasone will continue to avoid operative intervention for a minimum of 5 years.

Ng et al (163) studied periradicular infiltration of nerve roots with local anesthetic and steroid versus local anesthetic alone. They evaluated 86 patients with unilateral leg pain and an MRI showing a lumbar herniated disc or foraminal stenosis at a level compatible with the symptoms. All the patients received a single level injection under fluoroscopy with 2 mL of 0.25% bupivacaine with 40 mg of methylprednisolone in 1 group and the second group receiving only bupivacaine alone. The results showed no significant difference between the groups. In both groups, there was only a modest decrease in VAS at 3 months. Criticism of this study is that only 1 injection was offered.

Karppinen et al (165,166) evaluated transforaminal epidural steroid injections in patients with MRI-confirmed herniated nucleus pulposus. The outcome measures were 50% relief of leg pain and cost effectiveness. Vad et al (169) evaluated transforaminal epidural steroid injections and compared them to

patients undergoing lumbar paraspinal trigger point injections with sodium chloride solution. The outcome measures included improvement in leg pain, Roland-Morris score, and patient satisfaction score.

Thomas et al (170) evaluated the effectiveness of transforaminal epidural and compared it with interspinous corticosteroid injection. Devulder et al (167) used a combination of methylprednisolone, bupivacaine, and hyaluronidase and compared this to a combination of sodium chloride solution, bupivacaine, and hyaluronidase. The outcome measures were reduction in leg pain of at least 50%.

Kolstad et al (174) studied cervical transforaminal epidural steroids on 21 patients awaiting cervical disc surgery. Patients were given 2 epidural injections 2 weeks apart, and followed for 4 months. Three outcome assessments were performed at baseline, 6 weeks, and 4 months. Outcome measures included visual analogue scale pain intensity (0-100 mm) for neck pain, visual analogue scale pain intensity (0-100 mm) for radicular pain, and Odom's Criteria—a grading system to evaluate relief of symptoms and treatment satisfaction (1: Excellent, 2: Good, 3: Fair, 4: Poor). Five of the 21 patients canceled their surgery due to improvement in pain, and overall there was a significant decrease in radicular pain at 6 weeks and 4 months. Neck pain also improved, and patients with spondylosis responded as well as patients with disc herniations.

Among the prospective evaluations, the effect of transforaminal epidural steroids on candidates for discectomy was studied by Yang et al (175). They evaluated 21 lumbar radiculopathy patients, all of whom had CT or MRI visualized disc herniations, all of whom were felt to be candidates for discectomy. Sixty-three percent of the patients had significant pain relief lasting through the 24-month follow-up, avoiding surgery; the transforaminal epidural resulted in significant relief of leg pain and improvement in activities of daily living, but did not improve low back pain.

A retrospective review of cervical transforaminal steroid injections was published by Lin et al (130). They evaluated 70 patients in a retrospective evaluation with cervical disc herniation without myelopathy. The average follow-up was 13 months (6 months to 4 years), and the number of injections ranged from 1 to 4 (mean 1.46). At 1-year follow-up 63% of the patients had improved and avoided surgery.

Cost Effectiveness

Cost effectiveness of transforaminal epidural steroid injections in the management of chronic low

back pain showed that cost per 1-year improvement of quality of life was \$2,927 per year (85). Further, in patients treated with transforaminal steroids, operations were avoided for contained herniations, costing \$12,666 less per responder in the steroid group (166). Cost effectiveness was also demonstrated by avoiding surgical intervention (130,162,164,174).

Level of Evidence

The evidence for lumbar transforaminal epidural steroid injections in managing lumbar nerve root pain is strong for short-term and moderate for long-term improvement. The evidence for cervical transforaminal epidural steroid injections in managing cervical nerve root pain is moderate for short-term and long-term improvement. The evidence is limited in managing lumbar radicular pain in postlumbar laminectomy syndrome. The evidence is indeterminate in managing axial low back pain, axial neck pain, and lumbar disc extrusions.

Caudal Epidural Injections

Relevant reports studying caudal epidural injections included 11 randomized (99,207-216), 5 prospective evaluations (217-221), and multiple retrospective evaluations (3,16-19,84,85,222-224). The results of published reports of the randomized trials are described in Table 7, while Table 8 shows descriptions of prospective evaluations.

Of the 11 randomized trials, 3 trials were excluded (208,212,213). One study (213) was excluded due to non-availability of analyzable information, whereas a second trial (212) was excluded due to lack of long-term data. A recent study (208) was excluded due to poor protocol design and short-term relief and lack of fluoroscopy in the modern era.

Of the 8 randomized trials, 6 trials predominantly evaluated patients with disc herniation or radiculitis (99,207,209-211,214), 2 trials evaluated patients suffering with pain following failed back surgery syndrome (215,216), and one study (214) evaluated a mixed population with 50% postlumbar laminectomy syndrome patients. One study (99) compared blind interlaminar epidurals with caudal epidural steroid injections. One study (208) evaluated the effectiveness of triamcinolone acetonide and methylprednisolone acetate.

Among the 5 nonrandomized evaluations (217-221), disc herniation or radiculitis patients were studied in 2 evaluations (219,220), the role of caudal epidural in chronic low back pain was studied in an additional

2 studies (217,218), and the role of caudal epidural steroids was studied in spinal stenosis in one study (221).

Description of Study Characteristics

Descriptive characteristics of the included randomized trials are shown in Table 7 and non-randomized trials in Table 8.

Dashfield et al (207) compared the effectiveness of caudal steroid epidural with targeted steroid placement during spinal endoscopy for chronic sciatica in a prospective, randomized, double-blind trial. They studied 60 patients referred to their clinic for management of sciatica of greater than 6 months but less than 18 months' duration. The sciatica was defined as pain in the distribution of a lumbar nerve root, accompanied by neurosensory and motor deficits, with or without low back pain. Patients were 18 years of age or older. Patients who had previous spinal surgery, coagulopathy, progressive motor neuron disorders, or peripheral

vascular disease were excluded, as were patients who had received an epidural corticosteroid injection within 3 months of being randomized. Patients were allocated randomly into 2 groups. Patients in the caudal group underwent caudal epidural corticosteroid injection with a total of 10 mL of lidocaine 1% with 40 mg of triamcinolone being injected into the epidural space. Patients in the epiduroscopy group underwent epiduroscopy performed by an experienced epiduroscopist with placement of steroid over the nerve root, which included 10 mL of lidocaine 1% with triamcinolone 40 mg. The epiduroscopy group also received infusion of 50 to 150 mg mL of sodium chloride solution. If adhesions were encountered around the painful nerve root, an attempt was made to break adhesions down using saline boluses or by manipulating the endoscope. However, very little scar tissue was encountered in their patient population, as they never had previous surgery.

Table 7. Characteristics of published randomized trials of caudal epidural injections.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Dashfield (207) Prospective, randomized, double-blind trial AHRQ score: 9/10 Cochrane score: 8/10	60 pts presenting to the pain management center.	Corticosteroid injection with a total of 10 mL of lidocaine 1% with 40 mg of triamcinolone Epiduroscopy group: delivery of the medication over the painful nerve root with 10 mL of lidocaine 1% with 40 mg of triamcinolone.	Assessments: 6 wks, 3 mos, and 6 mos . Outcome instruments: SF-MPQ and HAD.	Caudal group: significant improvements were found for descriptive pain at 6 mos; VAS at 6 wks, 3 mos, and 6 months; present pain intensity at 3 mos and 6 mos; anxiety at 6 wks, 3 mos, and 6 mos; and depression at 6 mos only.	Positive short-term and long-term relief
McGregor et al (99) Prospective AHRQ score: 6/10 Cochrane score: 5/10	44 pts with low back and leg pain.	Caudal epidural vs lumbar epidural.	Visual Analog Scale.	No significant improvement.	Negative short-term and long-term relief
Breivik et al (209) Randomized, double-blind trial AHRQ score: 8/10 Cochrane score: 7/10	35 pts with incapacitating chronic low back pain and sciatica. Diagnosis based on radiculopathy: arachnoiditis (n=8), no abnormality (n=11), inconclusive findings (n=5). Duration: several mos to several yrs.	Caudal epidural injection: Experimental: 20 mL bupivacaine 0.25% with 80 mg depomethylprednisone (n=16) Placebo: 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: significant diminution of pain and/or paresis to a degree that enabled return to work. 2. Objective improvement: sensation, Lasègue's test, paresis, spinal reflexes, and sphincter disorders.	56% of the pts reported considerable pain relief in experimental group compared to 26% of the pts in the placebo group.	Positive short-term and long-term relief

Table 7 Continued. *Characteristics of published randomized trials of caudal epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Bush and Hillier (210) Randomized, double-blind trial AHRQ score: 8/10 Cochrane score: 8/10	23 pts with lumbar nerve root compromise randomized into 2 groups.	Experimental: 25 mL: 80 mg triamcinolone acetate + 0.5% procaine hydrochloride (n=12); Control: 25 mL normal saline (n=11). Frequency: two caudal injections, the first after admission to the trial and a second after 2 wks.	Timing: 4 wks and at 1 year. Outcome measures: 1. Effect on lifestyle; 2. Back and leg pain; 3. Angle of positive SLR.	Significantly better results with pain and straight leg raising in experimental group in short-term. Pain not significantly different but straight leg raise significantly better for long-term relief.	Positive short-term and negative long-term relief
Matthews et al (211) Randomized, double-blind trial AHRQ score: 8/10 Cochrane score: 7/10	57 pts with sciatica with a single root compression Experimental group: male/female: 19/4, median duration of pain: 4 wks. Control group: male/female: 24/10, median duration of pain: 4 wks.	Experimental: 20 mL bupivacaine 0.125% + 2 mL (80 mg) methylprednisolone acetate (n=23). Control: 2 mL lignocaine (over the sacral hiatus or into a tender spot) (n=34) Frequency: fortnightly intervals, up to 3 times as needed.	Timing: 2 wks, 1, 3, 6, and 12 mos. Outcome measures: pain (recovered vs not recovered), range of movement, straight leg raising, neurologic examination.	There was no significant difference between experimental and control group with short-term relief (67% vs 56%). After 3 mos, pts in experimental group reported significantly more pain-free than in control group.	Negative short-term and positive long-term relief
Helsa and Breivik (214) Randomized, double-blind trial with crossover design AHRQ score: 7/10 Cochrane score: 7/10	69 pts with incapacitating chronic low back pain and sciatica. 36 of 69 previously been operated on for herniated disc.	Three caudal epidural injections of either bupivacaine with depomethylprednisolone 80 mg or with bupivacaine followed by normal saline.	Timing: not mentioned. Outcome measures: significant improvement to return to work or to be retrained for another occupation.	34 of the 58 pts (59%) receiving caudal epidural injections of bupivacaine and depomethylprednisolone showed significant improvement. 12 of 49 pts (25%) who received bupivacaine followed by saline were improved.	Positive short-term and long-term relief.
Revel et al (215) Randomized trial AHRQ score: 7/10 Cochrane score: 6/10	60 postlumbar laminectomy pts with chronic low back pain.	Forceful caudal injection: Experimental: 125 mg of prednisolone acetate with 40 mL of normal saline in the treatment group. Control: 125 mg of prednisolone in the control group.	Timing: 6 mos. Outcome measures: pain relief.	The proportion of pts relieved of sciatica was 49% in the forceful injection group compared to 19% in the control group with significant difference.	Positive short-term and negative long-term relief
Meadeb et al (216) Randomized trial Parallel-group study AHRQ score: 6/10 Cochrane score: 6/10	47 postlumbar laminectomy syndrome pts in a multicenter study.	Experimental: forceful injection of 20 mL of normal saline with/without 125 mg of epidural prednisolone acetate. Control: 125 mg of epidural prednisolone. Frequency: each of the 3 treatments were provided once a month for 3 consecutive mos.	Timing: day 1, day 30, and day 120. Outcome measures: Visual Analog Scale.	The VAS scores improved steadily in the forceful injection group, producing a nonsignificant difference on day 120 as compared to the baseline (day 30=120 days).	Negative short-term and long-term relief.

Epidural Steroids in the Management of Chronic Spinal Pain

Table 8. Characteristics of results of prospective studies of caudal epidural injections.

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Yates (219) Prospective evaluation AHRQ score: 5/8	20 pts with low back pain and sciatica.	Group I: 60 mg of triamcinolone (3 mL + 47 mL normal saline). Group II: 60 mg of triamcinolone (3 mL + 47 mL lignocaine 0.5%). Group III: 50 mL saline. Group IV: 50 mL lignocaine injections given at weekly intervals in random order.	Timing not mentioned. Subjective and objective criteria of progress. Did not address pain-relief, focused on improvement in straight leg raising which seemed to correlate with pain-relief.	Greatest improvement was noted after the injection-containing steroid. The results suggested that the action of a successful epidural injection is primarily anti-inflammatory and to a lesser extent, hydrodynamic.	Positive short-term and long-term relief
Waldman (220) Prospective evaluation with independent observer review AHRQ score: 5/8	53 pts meeting stringent inclusion criteria with radicular pain distribution anatomically correlating with documented disc herniation and nerve root impingement.	Treatment: 7.5 mL of 1% lidocaine and 80 mg of methylprednisolone with the first block and 40 mg of methylprednisolone with subsequent blocks, which were repeated in 48- to 72-hour intervals with the end point being complete pain relief or 4 caudal epidural blocks.	Timing: 6 wks, 3 mos, and 6 mos. Visual Analog Scale and Verbal Analog Scores.	Combined Visual Analog Scale and Verbal Analog Scores for all pts were reduced 63% at 6 wks, 67% at 3 mos, and 71% at 6 mos.	Positive short-term and long-term relief
Manchikanti et al (217) Randomized trial with convenient control group. AHRQ score: 5/10	70 pts after failed conservative management with physical therapy, chiropractic, and medication therapy. All pts were shown to be negative for facet joint pain.	Group I : no treatment Group II: local anesthetic and Sarapin total of 20 mL with 10 mL each. Group III: 10 mL of local anesthetic and 6 mg of betamethasone.	Timing: 2 wks, 1 month, 3 mos, 6 mos, and 1 year. Outcome measures: Average pain, physical health, mental health, and functional status.	Average pain, physical health, mental health, functional status, narcotic intake, and employment improved significantly in Group II and Group III at 2 wks, 1 month, 3 mos, 6 mos, and 1 year.	Positive short-term and long-term relief
Manchikanti et al (218) Prospective evaluation AHRQ score: 5/8	62 pts evaluated. Negative provocative discography: 45 pts. Positive provocative discography: 17 pts.	Caudal epidural injections (1-3) with or without steroids.	Timing: 1 month, 3 mos, and 6 mos. Outcome: average pain, functional status, psychological status, narcotic intake, and employment status.	69% of the pts in the negative discography group and 65% of the pts in the positive discography group were in successful category.	Positive short-term and long-term relief
Ciocon et al (221) Prospective evaluation in elderly pts AHRQ score: 5/8	30 pts with spinal stenosis.	A series of 3 caudal epidural steroid injections, 0.5% xylocaine and 80 mg of Depo-Medrol.	Pain relief, Roland Morris 5-point scale.	Duration of pain relief and improvement ranged from 4-10 months.	Positive short-term and long-term relief.

Patient assessments were carried out before treatment, at 6 weeks, 3 months, and 6 months following treatment. Outcome instruments included SF-MPQ and HAD scores. No significant differences were found between the groups for any of the measures at any time. However, there were significant differences within both groups compared with pretreatment values. For the caudal group, significant improvements were found for descriptive pain at 6 months; VAS at 6 weeks, 3 months, and 6 months; present pain intensity at 3 months and 6 months; anxiety at 6 weeks, 3 months, and 6 months; and depression at 6 months only. Caudal epidural was better than the epiduroscopy group where there were fewer significant changes.

Effectiveness

Of the 8 randomized trials, 5 were positive for short-term pain relief (207,209,210,214,215), and 4 were positive for long-term relief (207,209,211,214).

Among 8 randomized trials included for analysis, of the 6 trials (99,207,209-211,214) evaluating predominantly radiculopathy, 4 studies were positive (207,209,210,214) and 2 were negative (99,211) for short-term relief, whereas 4 (207,209,211,214) of 6 (99,207,209-211,214) were positive for long-term relief. Of the 2 studies with postlumbar laminectomy syndrome (215,216), only one study (215) was positive for short-term. One study (214) included patients with sciatica, as well as post lumbar laminectomy syndrome. This study showed positive results, both for short-term and long-term.

Among the 5 prospective studies (217-221), 2 studies evaluating radiculopathy or sciatica (219,220) and 2 studies evaluating the effectiveness of caudal epidural steroid injections in chronic low back pain (217,218) were positive, and 1 study evaluating the effectiveness of caudal in lumbar spinal stenosis was positive (221).

Thus, positive long-term relief trials were 71% for radiculopathy or sciatica and 67% for postlumbar laminectomy syndrome. Among the prospective evaluations, 80% were positive for radiculopathy and chronic low back pain.

Cost Effectiveness

The costeffectiveness of fluoroscopically-directed caudal epidural steroids was \$3,635 and that of transforaminal steroids was \$2,927 per year. In a prospective evaluation, the cost for 1-year improvement for quality-of-life, was \$2,550, in patients treated with caudal epidural with local anesthetic and Sarapin or steroids under fluoroscopy (85,217).

Level of Evidence

The evidence of caudal epidural steroid injections with randomized trials and non-randomized reports is strong for short-term relief and moderate for long-term relief in managing chronic pain of lumbar radiculopathy and postlumbar laminectomy syndrome. The evidence is moderate in managing chronic low back pain for short-term and long-term improvement.

Complications

The most common and worrisome complications of caudal, interlaminar, and transforaminal epidural injections are of 2 types: those related to the needle placement and those related to drug administration. Complications include dural puncture, spinal cord trauma, infection, hematoma formation, abscess formation, subdural injection, intracranial air injection, epidural lipomatosis, pneumothorax, nerve damage, headache, death, brain damage, increased intracranial pressure, intravascular injection, vascular injury, cerebral vascular or pulmonary embolus, and effects of steroids (228-291). Spinal cord trauma, and spinal cord or epidural hematoma formation is a catastrophic complication that is rarely seen following interventional procedures in the cervical spine, thoracic spine, or upper lumbar spine.

Botwin et al (225-228) evaluated complications of fluoroscopically-guided epidural steroid injections. Botwin et al (225) reported complications in 207 patients receiving 322 injections of transforaminal lumbar epidural injections. Complications included transient headaches (3.1%), increased back pain (2.4%), increased leg pain (0.6%), facial flushing (1.2%), vasovagal reaction (0.3%), increased blood sugar (0.3%), and hypertension (0.3%). The incidence of minor complications was 9.6% per injection with no major complications.

Botwin et al (226) reported complications of fluoroscopically-guided interlaminar cervical epidural injections. They reported 345 injections in 157 patients. Complications per injection included increased neck pain (6.7%), non-positional headaches (4.6%), insomnia the night of injection (1.7%), vasovagal reactions (1.7%), facial flushing (1.5%), fever the night of the procedure (0.3%), and dural puncture (0.3%). The incidence of all complications per injection was 16.8%.

Botwin et al (227) also reported adverse effects of fluoroscopically guided interlaminar thoracic epidural steroid injections. A total of 21 patients received 39 injections. Adverse effects or complications per injection observed included pain at injection site (7.7%), facial flushing (5.1%), transient non-positional head-

ache (2.6%), insomnia the night of injection (2.6%), and fever the night of the procedure (2.6%). No major complications were reported and adverse effects were reported with a rate of 20.5%.

Botwin et al (228) reported complications of fluoroscopically-guided caudal epidural injections in 139 patients, who received 257 injections. Complications per injection included insomnia the night of injection (4.7%), transient non-positional headaches (3.5%), increased back pain (3.1%), facial flushing (2.3%), vasovagal reactions (0.8%), nausea (0.8%), and increased leg pain (0.4%). The incidence of minor complications was 15.6% per injection.

Furman et al (229) evaluated incidence of intravascular penetration in transforaminal lumbosacral epidural steroid injections in a prospective observational study. Among the 761 transforaminal epidural steroid injections included in the study, the overall rate of intravascular injections was 11.2%, with a higher rate of intravascular injections (21.3%) noted with transforaminal epidural injections at S1 compared with those at the lumbar levels (8.1%).

Furman et al (230) also studied incidence of intravascular penetration in transforaminal cervical epidural steroid injections in 307 patients with 504 treated with transforaminal epidural steroid injections. The overall rate of fluoroscopically-confirmed intravascular contrast injections was 19.4%.

Manchikanti et al (231) reported contrast flow patterns and intravascular needle placement in 100 consecutive patients. Intravenous placement of the needle was noted in 22% of the procedures. With caudal epidurals, Manchikanti et al (231) reported complications with pain during the injection with back pain in 43% of the patients and leg pain in 22% of the patients. They also noted postoperative complications in 34% of the patients with soreness at injection site in 18%, increased pain in 5%, muscle spasms in 4%, swelling in 4%, headache in 3%, minor bleeding in 2%, dizziness in 1%, nausea and vomiting in 1%, fever in 1%, numbness in 1%, and voiding difficulty in 1%. Manchikanti et al (232,233) reported with fluoroscopically-guided caudal epidural injections intravascular placement in 14% of the patients. They (232,233) also reported complications in 7% of the patients with soreness at injection site in 6%, increased pain in 1%, muscle spasms in 1%, headache in 1%, and nausea and vomiting in 1%.

Derby et al (234) surveyed 17 International Spinal Intervention Society (ISIS) instructors who described

a total of 5,978 cervical epidurals, interlaminar in 4,389 patients, and transforaminal injections in 1,579 patients. Of the interlaminar injections, there were 23 mild complications (0.5%), while there were 5 cases of minor complications in the transforaminal group (0.32%).

Transforaminal injections have been the cause of some of the most worrisome recent complications. These included cerebellar and cerebral infarct (235,247), spinal cord injury and infarction (236,245,249,256), massive cerebral edema (237), paraplegia (238), visual defects with occlusion following particulate depo-corticosteroids (239), anterior spinal artery syndrome (240), persistent neurological deficits (241), transient quadriplegia (242), cauda equina syndrome (251), subdural hematoma (253), and paraplegia following intracord injection during attempted epidural anesthesia under general anesthesia (255).

Because of the catastrophes associated with cervical transforaminal epidurals, Huntoon (243) dissected 95 nerve roots in 10 embalmed cadavers. He was able to identify 21 foramina where an artery was noted to be proximal to the posterior aspect of the foraminal opening, confirming the potential for injury to a vessel during transforaminal injections.

Although the complications of cervical spinal injections are devastating, they are fortunately rare. Ma et al (244) reviewed the complications of 1,036 fluoroscopically-guided extraforaminal cervical nerve blocks performed on 844 patients over a 4-year period, and found only 14 patients (1.66%) who had even minor complications.

Huston et al (246) reviewed complications of cervical and lumbar selective nerve root injections (SNRs) in 151 consecutive patients who underwent a total of 306 SNRs. There were no major complications noted, and 91% of the patients had no side effects during the injection. The most common side effect noted was increased pain at the injection site after the injection, which was seen in 17.1% of the lumbar patients and 22.7% of the cervical patients.

Paraplegia and quadriplegia have also been reported following interlaminar epidural steroid injections (252).

Infection is occasionally seen with a case of granuloma and intracranial hypertension after 3 cervical epidural steroids (258), thoracic intradural fungal abscess after 3 lumbar epidural steroids (259,270), discitis (267-269,272), and numerous cases of epidural hematoma over the years (262-266).

Other much less common complications include pneumocephalus (273,275,286), transient blindness

(276), retinal necrosis (277), bilateral cirrus chorioretinopathy (278,279), persistent recurrent intractable hiccups (280), dysphonia (281), flushing (282), arterial gas embolus and cortical blindness (283,284), chemical meningitis (287), retinal hemorrhage (288), radiculopathy (289), nerve root damage (290), and cerebral venous thrombosis (291).

Side effects related to the administration of steroids are generally attributed either to the chemistry or to the pharmacology of the steroids. The major theoretical complications of corticosteroid administration include suppression of pituitary-adrenal axis, hypercorticism, Cushing's syndrome, osteoporosis, avascular necrosis of bone, steroid myopathy, epidural lipomatosis, weight gain, fluid retention, and hyperglycemia. The most commonly used steroids in neural blockade in the United States, methylprednisolone acetate, triamcinolone acetonide, betamethasone acetate, and phosphate mixture have all been shown to be safe at epidural therapeutic doses in both clinical and experimental studies (292-301).

Finally, radiation exposure is also a potential problem with damage to eyes, skin, and gonads (302-304).

Discussion

This systematic review evaluated and updated the effectiveness of epidural injections in patients with chronic spinal pain. The evidence was evaluated for 3 types of epidurals separately for cervical and lumbar, and for axial, radicular, and postlaminectomy pain.

The previous systematic review arrived at the following conclusions (3). In managing lumbar radicular pain with interlaminar lumbar epidural steroid injections, the level of evidence was strong for short-term relief and limited for long-term relief. In managing cervical radiculopathy with cervical interlaminar epidural steroid injections, the evidence was moderate for short-term improvement and long-term improvement. However, the evidence was indeterminate in management of axial neck pain, axial low back pain, and lumbar spinal stenosis with lumbar or cervical interlaminar epidural steroid injections.

The evidence for lumbar transforaminal epidural steroid injections in managing lumbar nerve root pain was strong with short-term and long-term improvement. The evidence for cervical transforaminal epidural steroid injections in managing cervical nerve root pain was strong with short-term and long-term improvement. The evidence was moderate in managing lumbar radicular pain in postlumbar laminectomy syndrome,

with short-term and long-term improvement. The evidence of lumbar transforaminal epidural steroid injections in managing lumbar spinal stenosis was limited. The evidence was indeterminate in managing axial low back pain, axial neck pain, and lumbar disc extrusions.

The evidence of caudal epidural steroid injections with randomized trials and non-randomized reports was strong for short-term relief and moderate for long-term relief, in managing chronic pain of lumbar radiculopathy and postlumbar laminectomy syndrome. The evidence was moderate in managing chronic low back pain for short-term and long-term improvement. The evidence was limited for lumbar spinal stenosis.

The first systematic review of effectiveness of epidural steroid injections was performed by Kepes and Duncalf in 1985 (5). They concluded that the rationale for epidural and systemic steroids was not proven. However, in 1986 Benzon et al (297), utilizing the same studies, concluded that mechanical causes of low back pain, especially those accompanied by signs of nerve root irritation, may respond to epidural steroid injections. The difference in the conclusion of Kepes and Duncalf (5) and Benzon et al (297) may have been due to the fact that Kepes and Duncalf (5) included studies on systemic steroids whereas Benzon (297) limited their analysis to studies on epidural steroid injections only.

The debate concerning epidural steroid injections is also illustrated by the recommendations of the Australian National Health and Medical Research Council Advisory Committee on epidural steroid injections (84). In this report, Bogduk (10) extensively studied caudal, interlaminar, and transforaminal epidural injections, including all the literature available at the time, and concluded that the balance of the published evidence supports the therapeutic use of caudal epidurals. They also concluded that the results of lumbar interlaminar epidural steroids strongly refute the utility of epidural steroids in acute sciatica. Bogduk et al (84) updated their recommendations in 1999, recommending against epidural steroids by the lumbar route because effective treatment required too high a number for successful treatment, but supporting the potential usefulness of transforaminal steroids for disc prolapse. In 1995, Koes et al (6) reviewed 12 trials of lumbar and caudal epidural steroid injections and reported positive results from only 6 studies. However, review of their analysis showed that there were 5 studies for caudal epidural steroid injections and 7 studies for lumbar epidural steroid injections. Four of the 5 studies involving caudal epidural steroid injections were positive, whereas 5 of 7 studies

were negative for lumbar epidural steroid injections. Koes et al (7) updated their review of epidural steroid injections for low back pain and sciatica, including 3 more studies with a total of 15 trials which met the inclusion criteria. In this study, they concluded that of the 15 trials, 8 reported positive results of epidural steroid injections. Both reviews mostly reflected the quality of studies, rather than any meaningful conclusion.

Nelemans et al's (8) Cochrane review of injection therapy for subacute and chronic benign low back pain included 21 randomized trials. Of these, 9 were of epidural steroids. They failed to separate caudal from interlaminar epidural injections, but still concluded that convincing evidence is lacking regarding the effects of injection therapy on low back pain. Rozenberg et al (9), in a systematic review, identified 13 trials of epidural steroid therapy. They concluded that 5 trials demonstrated greater pain relief within the first month in the steroid group as compared to the control group. Eight trials found no measurable benefits. They noticed many obstacles for meaningful comparison of cross studies, which included differences in the patient populations, steroid used, volume injected, and number of injections. These authors were unable to determine whether epidural steroids are effective in common low back pain and sciatica based on their review. Rozenberg et al (9) concluded that 3 of the top 5 rated studies did not demonstrate significant benefit of the steroid over the non-steroid group. Hopayiank and Mugford (305) expressed frustration over the conflicting conclusions from two systematic reviews of epidural steroid injections for sciatica and asked which evidence should general practitioners heed. Multiple previous reviews have criticized the studies evaluating the effectiveness of epidural injections. Criticisms ranged from methodology, small size of the study populations, and other limitations, including long-term follow-up and outcome parameters.

Overall the evidence for lumbar interlaminar epidural steroid injections is limited for long-term relief. However, for cervical interlaminar epidural steroid injections, the evidence is moderate. Evidence is indeterminate in management of the axial neck pain, axial low back pain, and lumbar spinal stenosis with lumbar or cervical interlaminar epidural steroid injections.

In this study, the evidence for lumbar transforaminal epidural steroid injections in managing lumbar and cervical nerve root pain is moderate; however, the evidence is limited in managing lumbar radicular pain in postlumbar laminectomy syndrome. The evidence is

indeterminate in managing axial low back pain, neck pain, and lumbar disc extrusions.

The evidence of caudal epidural steroid injections is moderate in managing lumbar radiculopathy and postlumbar laminectomy syndrome. In contrast to interlaminar and transforaminal epidural injections the evidence is moderate in managing chronic low back pain. Airaksinen et al (11) in European Guidelines for the Management of Chronic Nonspecific Low Back Pain, published in 2006, which only included the literature up to 2002, concluded that epidural corticosteroid injections would only be considered for radicular pain if it contained disc prolapse as the cause of the pain and if the corticosteroid is injected close to the target or the nerve root. In addition, they also stated that the injection should be fluoroscopically-guided and should aim at the ventral part of the epidural space, near the spinal nerve root or the spinal nerve root through a transforaminal approach. They also concluded that there is conflicting evidence that conventional epidural steroids with a blind approach without fluoroscopic guidance are effective in radicular pain.

The present review is similar to 2 previous systematic reviews and also the guidelines published (16-19). However, it is vastly different from a multitude of other systematic reviews. It is close to European Guidelines for the Management of Chronic Nonspecific Low Back Pain, which advises that fluoroscopically-guided epidurals have better prognosis than the blind epidurals. The present systematic review, similar to the ones performed by Abdi et al (3) and Boswell et al (4), has several additional features.

Finally, all types of epidural steroid injections can be associated with complications and adverse events as described earlier. Therefore attention to detail and caution should be taken when performing any of the 3 techniques discussed in order to improve safety and minimize complications.

This systematic review included multiple new articles not described in the previous reviews.

Arden's study (120) compared 10 mL of epidural bupivacaine and steroid to 2 mL normal saline in the interspinous ligament. The use of local anesthetic in one and not the other makes true patient blinding unlikely. Wilson-MacDonald (119) injected the same local and steroid into each patient, either epidurally or in the ligament, but the large volume injected (8 mL) would be expected to be very painful and disruptive in the relative closed space of the interspinous ligament, again calling the patient blinding into ques-

tion. Therefore no significant new information can be gathered from these 2 studies. They also published 2 different manuscripts from 1 study.

In the 2 new cervical transforaminal studies, Kolstad et al (174) and Line et al (130) both showed that cervical epidural transforaminal injections can lead to pain relief significant enough to prevent patients from having to undergo surgery. Yang et al (175) also concluded that lumbar transforaminal injections reduce the need for lumbar surgical decompression.

One could argue that scientific evidence supporting the efficacy of transforaminal epidural steroid injection indirectly supports the efficacy of epidural administration by any route of administration. This argument makes sense in view of the anatomy of the epidural space and the pathophysiology of radiculopathy. To elaborate, the epidural space is a continuous anatomic compartment extending from the base of the skull to the sacrum that can be entered at various levels and by various routes to achieve the same end. The space itself consists of adipose tissue interspersed with random bands of fibrous tissue and venous vessels. The ventral epidural space is closest to the posterior disc margin and the traversing nerve root, which is the presumed site of pathology in lumbar radiculopathy. Although the most direct method to deposit medication into this region is by using a transforaminal approach to needle insertion, it is conceivable that medication may reach this target equally well using a caudal, interlaminar, or

catheter route of administration.

Regarding pathophysiology, investigations into the biochemistry of disc degeneration and herniation indicate that intraspinal inflammation is a major cause of radicular pain (253,255-257,272,283,284). The neurotoxic, inflammatory mediator phospholipase A2 (PLA2) is contained within the disc nucleus and is released after annular injury. PLA2 in turn triggers the arachidonic acid cascade, leading to localized inflammation mediated by prostaglandins and leukotrienes. Inflammatory neuropeptides such as calcitonin gene-related peptide (CGRP) and substance P are contained within the dorsal root ganglion and perpetuate inflammation as they are released from irritated nerve roots. Corticosteroids have powerful anti-inflammatory effects, which include inhibition of prostaglandin synthesis, blockade of PLA2 activity, and stabilization of inflammatory cell membranes. Injecting corticosteroids into the epidural space should result in higher concentrations of the active medication at the site of inflammation when compared to oral or parenteral routes of steroid administration. The spinal injection route of administration is the only method of drug delivery that does not rely on blood flow to deliver the medication to its site of action and blood flow may be impaired in the region of compressive disc herniation. Even with normal spinal circulation, blood flow delivers steroid preferentially to high blood flow organs with presumably low concentrations arriving at the site of spinal pathology.

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