

## A SYSTEMATIC REVIEW

## EPIDURAL STEROIDS IN THE MANAGEMENT OF CHRONIC SPINAL PAIN AND RADICULOPATHY

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Epidural injections with or without steroids are used extensively in the management of chronic spinal pain. However, evidence is contradictory with continuing debate about the value of epidural steroid injections in chronic spinal syndromes.

The objective of this systematic review is to determine the effectiveness of epidural injections in the treatment of chronic spinal pain. Data sources include relevant literature identified through searches of MEDLINE, EMBASE (Jan 1966- Mar 2003), manual searches of bibliographies of known primary and review articles, and abstracts from scientific meetings. Both randomized and non-

randomized studies were included in the review based on the criteria established by the Agency for Healthcare Research and Quality (AHRQ). Studies were excluded from the analysis if they were simply review or descriptive and failed to meet minimum criteria.

The results showed that there was strong evidence to indicate effectiveness of transforaminal epidural injections in managing lumbar nerve root pain. Further, evidence was moderate for caudal epidural injections in managing lumbar radicular pain. The evidence in management of chronic neck pain, chronic low back pain, cervical radiculopathy, spinal stenosis, and post laminectomy syn-

drome was limited or inconclusive.

In conclusion, the evidence of effectiveness of transforaminal epidural injections in managing lumbar nerve root pain was strong, whereas, effectiveness of caudal epidural injections in managing lumbar radiculopathy was moderate, while there was limited or inconclusive evidence of effectiveness of epidural injections in managing chronic spinal pain without radiculopathy, spinal stenosis, post lumbar laminectomy syndrome, and cervical radiculopathy.

**Keywords:** Low back pain, epidural steroids, interlaminar, caudal, transforaminal, radiculopathy

Lifetime prevalence of spinal pain has been reported as 65% to 80% in the neck and low back (1-5). After the initial episode, modern evidence has shown that the prevalence of persistent low back and neck pain ranges from 26% to 75% (6-17). Patho-anatomic evidence shows that discs can produce pain in the neck and upper extremities; thoracic spine, chest wall and abdominal wall; and low back and lower extremities. Disc related pain is caused by disc degeneration, disc herniation, or by biochemical effects including inflammation. Human intervertebral disc degeneration is a formidable clinical problem and a leading cause of pain and disability, resulting in significant healthcare-related costs (18-22). The degenerative process in intervertebral discs is associated with a series of biochemical and morphologic changes that combine to alter the biomechanical properties of the motion seg-

ment (18, 22-25). Disc degeneration with or without disc herniation can cause low back pain (26-30).

Traditionally, compression of nerve roots or dorsal root ganglion by the herniated nucleus pulposus (HNP) has been regarded as the cause of sciatica, but during the past decade, the pivotal role of multiple etiologies has been implicated. Thus, proposed etiologies are not limited to neural compression (22, 26, 27), but also include vascular compromise (22, 31), inflammation (32-35), biochemical and neural mechanisms (18, 36-44), internal disc disruption (45), intraneural and epidural fibrosis (46-50), dural irritation (51), spinal stenosis (52), and inflammation and swelling of dorsal root ganglion (53-55).

Epidural injection of corticosteroids is one of the commonly used interventions in managing chronic spinal pain (56-58). Several approaches are available to access the lumbar epidural space: caudal, interlaminar, and transforaminal. Epidural administration of corticosteroids is one of the subjects most studied in interventional pain management with the most systematic reviews available, though highly controversial (59-71). Bogduk et al (57) in 1994,

after extensive review, concluded that the balance of the published evidence supports the therapeutic use of caudal epidurals. Bogduk (61) in 1999 supported the potential usefulness of transforaminal steroids for disc prolapse. Bogduk and Govind (72) in 1999 concluded that transforaminal injection of steroids can be entertained with the prospect of achieving substantial and lasting relief of the pain; but if facilities for transforaminal injections are not available, patients might be offered temporizing, palliative therapy by means of caudal injection of steroid and local anesthetic for patients with lumbar radicular pain unresponsive to lesser, conservative measures, and for whom surgery might be the only other option. Bogduk (73) in 1999, in reference to cervical radicular pain concluded that in the interest of helping patients avoid surgery when this is the only other therapeutic option being entertained, a cervical epidural injection of steroids might be offered, or preferably, if facilities are available, a periradicular injection of steroids might be offered. However, both of these recommendations (72, 73) apply to acute lumbar and cervical radicular pain. Bogduk and McGuirk (74) in reviewing monotherapy for chronic low back pain (not radicu-

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lar pain) concluded that epidural steroids may be indicated for radicular pain, but they are not indicated for acute back pain and there is no evidence that they are effective for chronic low back pain. Koes et al (62, 63) in a systematic review of randomized clinical trials concluded that the efficacy of epidural steroid injections has not yet been established and their benefit, if any, seems to be of short duration only. van Tulder et al (65, 75) in 1997 and 2000, concluded that there was conflicting evidence that epidural steroid injections provide better short-term pain relief than placebo for patients with radicular symptoms. Further, they concluded that there was moderate evidence that epidural steroid injections were not effective for chronic low back pain without radicular symptoms. Watts and Silagy (64) in a 1995 meta-analysis, concluded that epidural steroids were effective based on the definition of effectiveness in terms of pain relief (at least a 75% improvement) in the short-term (60 days) and in the long-term (1 year). McQuay and Moore (68) in 1998 concluded that epidural corticosteroid injections were effective for back pain and sciatica, providing substantial relief for up to 12 weeks, but few patients with chronic spinal pain reported complete relief with majority returning for repeated epidural injections. Nelemans et al (66) in 2001, in a Cochrane review of injection therapy, concluded that epidural steroid injections were not effective in management of chronic low back or radicular pain. Vroomen et al (69) in 2000, in a review of conservative treatment of sciatica, concluded that epidural steroids may be beneficial for subgroups of nerve root compression. Rozenberg et al (70) in 1999 were unable to determine whether epidural steroids are effective in common low back pain and sciatica based on their review. In contrast, Manchikanti et al (56, 58) in reviewing the literature in 2001 and 2003, reviewed three types of epidurals separately rather than in combination as the previous reviews. They concluded that there was favorable evidence for caudal epidural steroid injections and transforaminal epidural steroid injections in managing chronic low back pain. There are no systematic reviews available describing pain of cervical or thoracic origin.

Mechanism of action of epidural injections is not well understood. It is believed that neural blockade alters or interrupts nociceptive input, reflex mechanisms of the afferent limb, self-sustaining

activity of the neuron pools and neuraxis, and the pattern of central neuronal activities (76). Explanations for improvements are based in part on the pharmacological and physical actions of local anesthetics, corticosteroids, and other agents. It is believed that local anesthetics interrupt the pain-spasm cycle and reverberating nociceptor transmission, whereas corticosteroids reduce inflammation either by inhibiting the synthesis or release of a number of pro-inflammatory substances and by causing a reversible local anesthetic effect (77-90), even though an inflammatory basis for either cervical or radicular pain has not been proven (72, 73).

This systematic review was undertaken due to conflicting opinions and inconclusive evidence in the literature. Further, authors strongly believe that due to the inherent variations and differences in the 3 techniques applied in delivery of epidural steroids, previous reviews were not only incomplete, but also inaccurate. Thus, due to variations, differences, advantages, and disadvantages applicable to each technique (including the effectiveness and outcomes), caudal epidural injections; interlaminar epidural injections (cervical, thoracic, and lumbar epidural injections); and transforaminal epidural injections (cervical, thoracic, and lumbosacral) are considered as separate entities within epidural injections and are evaluated as such.

## METHODS

### Literature Search

Our literature search included MEDLINE, EMBASE (Jan 1966 – Mar 2003), systematic reviews, narrative reviews,

cross-references to the reviews and various published trials; and peer reviewed abstracts from scientific meetings during the past two years. The search strategy consisted of diagnostic interventional techniques, epidural injections and steroids, transforaminal epidurals, nerve root blocks, and caudal epidural steroids, with emphasis on chronic pain/low back pain/neck pain/mid back or thoracic pain or spinal pain.

### Selection Criteria

The review focused on randomized and non-randomized evaluations. The population of interest was patients suffering with chronic spinal pain for at least 3 months. Three types of epidural injections 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 and statistical evaluations were reviewed. The primary outcome measure was pain relief at various points. The secondary outcome measures were functional status improvement and complications.

For evaluating the quality of individual articles, we have used the criteria from the Agency for Healthcare Research and Quality (AHRQ) publication (91). This document described important domains and elements for randomized and non-randomized trials as shown in Table 1.

### Data Extraction

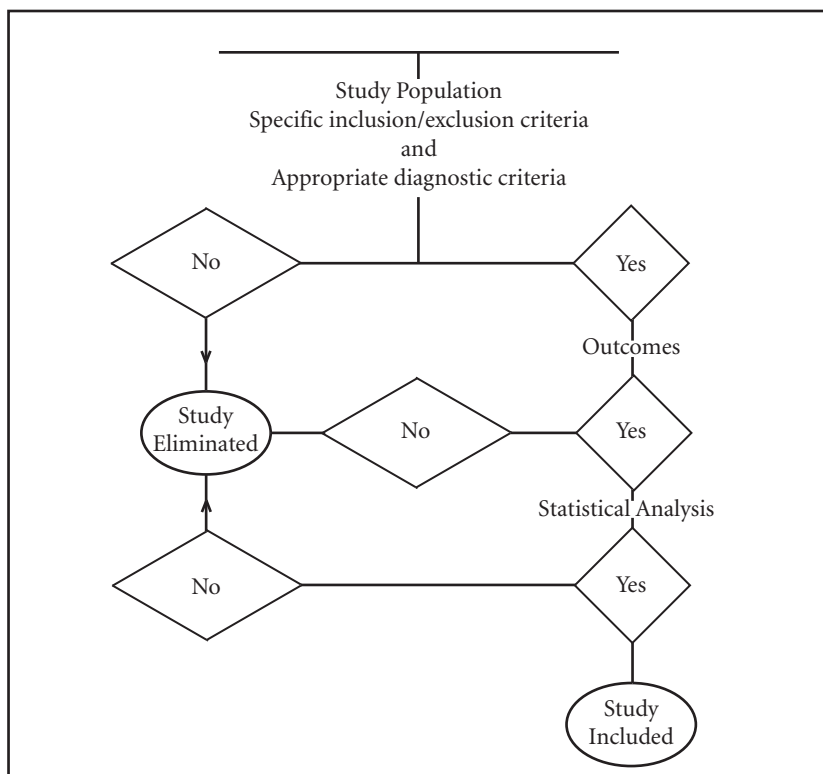
Study evaluation and inclusion and exclusion algorithmic approach is shown in Table 2. Methodologic quality assessment was performed as described in Table 1. A score of 4 or more of 7 for randomized trials and a score of 3 or more

Table 1. *AHRQ's important domains and elements for systems to rate quality of individual articles (91)*

Randomized Clinical Trials	Observational Studies
1. Study question	Study question
2. <i>Study population</i>	<i>Study population</i>
3. <i>Randomization</i>	<i>Comparability of subjects</i>
4. <i>Blinding</i>	
5. <i>Interventions</i>	<i>Exposure or intervention</i>
6. <i>Outcomes</i>	<i>Outcome measurement</i>
7. <i>Statistical analysis</i>	<i>Statistical analysis</i>
8. Results	Results
9. Discussion	Discussion
10. <i>Funding or sponsorship</i>	<i>Funding or sponsorship</i>

\* Key domains in italics

Table 2. Study evaluation (inclusion/exclusion) algorithm



of 5 was required to meet inclusion criteria. Studies were also eliminated if there were no appropriate outcomes of at least 3 months or statistical analysis.

Modified quality abstraction forms described by AHRQ were utilized. All the potential studies were evaluated by the 3 authors. Any disagreements were resolved by consensus.

**Qualitative Analysis**

Qualitative analysis was conducted, using five levels of evidence for effectiveness of epidural steroids as illustrated

in Table 3. Pain relief was evaluated on both a short-term (less than 3 months) and long-term (3 months 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 explanation.

Table 3. 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 one properly designed randomized, controlled trial of appropriate size (with at least 60 patients in smallest group); or research-based evidence from multiple properly designed studies of smaller size; or at least one randomized trial, supplemented by predominantly positive prospective and/or retrospective evidence.
Level III -	Moderate: Evidence from a well-designed small randomized trial or evidence from well-designed trials without randomization, or quasi-randomized studies, single group, pre-post cohort, time series, or matched case-controlled studies or positive evidence from at least one meta-analysis.
Level IV -	Limited: Evidence from well-designed nonexperimental studies from more than one center or research group
Level V -	Indeterminate: Opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committees.

**RESULTS**

**Caudal Epidural Injections**

Multiple reports studying caudal epidural injections included 8 randomized or double blind trials (92-99), 4 prospective trials (100-103), and multiple retrospective evaluations (104-107). The results of published reports of the randomized trials are described in Table 4, while Table 5 shows description of non-randomized trials (prospective and retrospective).

Of the 8 randomized or double blind trials, 2 trials were excluded. One study was excluded (96), due to non-availability of analyzable information. A second trial (95) was excluded due to lack of data at 3 months. Of the remaining 6 trials, 4 were positive for short-term pain relief (92, 93, 97, 98), and 4 were positive for long-term relief (92, 94, 97, 98). Among the 4 prospective trials (100-103) and 4 retrospective trials (104-107) meeting inclusion criteria, all were positive for short-term and long-term relief with multiple injections.

Among 6 randomized trials included for analyses (92-94, 97-99), only 3 studied predominantly patients with radiculopathy or sciatica (92-94), 2 studied post lumbar laminectomy syndrome (98, 99), and 1 studied mixed population (97). Of the 3 trials evaluating predominantly radiculopathy, 2 were positive (92, 93) and one study was negative (94) for short-term relief, whereas 2 of 3 were positive for long-term relief (92, 94). Among two studies with postlumbar laminectomy syndrome (98, 99), only one study (98) was positive in short-term and long-term. None of the studies included only the patients with chronic low back pain.

Among the non-randomized evaluations, including retrospective studies, four (102-104, 106) of eight (100-107) included patients with radicular pain or sciatica, all showing positive results. Three studies essentially included patients with chronic low back pain without demonstrated radicular pain (100, 101, 105). One study (107) evaluated the patients with lumbar canal stenosis.

**Interlaminar Epidural Injections**

Multiple studies evaluating the effectiveness of interlaminar epidural injections, specifically the lumbar epidural injections included 16 randomized or double blind trials (108-123), 8 non-randomized prospective trials (124-131),

Table 4. Characteristics of published randomized trials of caudal epidural injections

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/Conclusion
Brevik et al (92) Randomized double blind trial. Randomization according to a list of random numbers. Parallel, cohort design	35 patients 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 months to several years.	Caudal epidural injection: Experimental: 20 mL bupivacaine 0.25% with 80 mg depomethylprednisolone (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 patients reported considerable pain relief in experimental group compared to 26% of the patients in the placebo group.	Positive short-term and long-term relief
Bush and Hillier (93) Randomized double blind trial. 28 patients were randomized; only 23 patients were entered into the study.	23 patients with lumbar nerve root compromise. Mean duration (range) in experimental group: 5.8 months (1-13 months) and in control group 4.7 months (1-12).	Caudal epidural injections: 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 weeks	Timing: four weeks and at one 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 relief and negative long-term relief
Matthews et al (94) Double blind. Stratification by age and gender. Survival curve analyses based on cumulative totals recovered.	57 patients with sciatica with a single root compression Experimental group: male/female: 19/4, median duration of pain: 4 weeks (range: 8 days-3 months). Control group: male/female: 24/10, median duration of pain: 4 weeks (range: 3 days-9 weeks).	Caudal epidural injections: 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 three times as needed	Timing: 2 weeks, 1, 3, 6, and 12 months. Outcome measures: 1. Pain (recovered vs not recovered). 2. Range of movement 3. Straight leg raising 4. Neurologic examination	There was no significant difference between experimental and control group with short-term relief (67% vs 56%). After 3 months, patients in experimental group reported significantly more pain-free than in control group.	Negative short-term relief and positive long-term relief
Helsa and Brevik (97) Double blind trial with crossover design	69 patients 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. If no improvement had occurred after 3 injections, a series of the alternative type of injection was given.	Timing: not mentioned. Outcome measures: significant improvement to return to work or to be retrained for another occupation	i. 34 of the 58 patients (59%) receiving caudal epidural injections of bupivacaine and depomethylprednisolone showed significant improvement. ii. 12 of 49 patients (25%) who received bupivacaine followed by saline were improved.	Positive short-term and long-term relief
Revel et al (98) Randomized trial.	60 post lumbar laminectomy patients 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 months. Outcome measures: pain relief.	The proportion of patients relieved of sciatica was 49% in the forceful injection group compared to 19% in the control group with significant difference.	Positive short-term and long-term relief
Meadeb et al (99) Randomized trial. Parallel-group study.	47 post lumbar laminectomy syndrome patients in a multicenter study.	Experimental group: forceful injection of 20 mL of normal saline with or without 125 mg of epidural prednisolone acetate. Control group: 125 mg of epidural prednisolone. Frequency: each of the 3 treatments were provided once a month for 3 consecutive months.	Timing: day 1, day 30 and day 120. Outcome measures: visual analog scores.	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

Table 5. *Characteristics and results of non-randomized studies of caudal epidural injections*

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/Conclusion
Yates (102) Prospective evaluation	20 patients 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 were given at weekly intervals in a random order	Timing not mentioned. Subjective and objective criteria of progress. Study did not address pain-relief. Study 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 (103) Prospective evaluation with independent observer review.	53 patients 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. Subsequent blocks were repeated in 48 to 72 hour intervals with the end point being complete pain relief or 4 caudal epidural blocks.	Timing: 6 weeks, 3 months, 6 months. Visual analog scale and verbal analog scores.	Combined visual analog scale and verbal analog scores for all patients were reduced 63% at 6 weeks, 67% at 3 months, and 71% at 6 months.	Positive short-term and long-term relief.
Manchikanti et al (100) A randomized trial with convenient control group.	70 patients after failed conservative management with physical therapy, chiropractic and medication therapy. All patients were shown to be negative for facet joint pain.	Caudal epidural injections: 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 weeks, 1 month, 3 months, 6 months 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 weeks, 1 month, 3 months, 6 months and 1 year.	Positive short-term and long-term relief.
Manchikanti et al (101) Prospective evaluation in discogram-positive and discogram-negative chronic low back pain patients.	62 patients were evaluated. Negative provocative discography: 45 patients Positive provocative discography: 17 patients	Caudal epidural injections (1-3) with or without steroids.	Timing: 1 month, 3 months, and 6 months. Average pain, physical health, mental health, functional status, psychological status, symptom magnification, narcotic intake and employment status.	69% of the patients in the negative discography group and 65% of the patients in the positive discography group were in successful category. Comparison of overall health status, psychological status, narcotic intake and return to work showed significant improvement in successful category.	Positive short-term and long-term relief.
Hauswirth and Michot (104) Retrospective evaluation	75 patients with chronic low back pain and sciatica	Caudal epidural injections of local anesthetic and steroids	Timing: not mentioned Outcome measures: pain relief	Results were excellent in 60% and good in 24%. 16% of the patients showed no improvement.	Positive short-term and long-term relief.
Manchikanti et al (105) Retrospective evaluation of 225 patients with chronic low back pain.	Chronic pain patients who have failed to respond to conservative management with physical therapy, chiropractic and medical therapy.	Group I: Blind lumbar epidural steroid injections, Group II: Caudal epidural steroid injections under fluoroscopy. Group III: Transforaminal epidural corticosteroid injections under fluoroscopic visualization.	Duration of pain relief with each injection. Outcome measures: relief $\geq$ 50%	Cumulative significant relief, was reported following 3 procedures for a mean of 10.3 $\pm$ 0.96 weeks in patients receiving caudal epidurals, in contrast to 6.7 $\pm$ 0.37 weeks in patients receiving blind lumbar epidural steroid injections.	Positive short-term and long-term relief.

Table 5. Characteristics and results of non-randomized studies of caudal epidural injections (Continued)

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/Conclusion
Goebert et al (106) Retrospective evaluation of 113 patients.	113 patients at a tertiary care center receiving 120 injections. 94 were caudal epidural injections There were no objective signs present in the patients.	Epidural injections of 30 mL of 1% procaine combined with 125 mg of hydrocortisone acetate usually for 3 consecutive or alternate days.	Timing: 3 months Pain relief: Good result 60% relief for 3 months or longer Failures: 40% to 60% relief Poor results: return of pain in less than 3 months or less than 40% of relief.	Overall good results in 72% of the patients with poor results in 17%.	Positive short-term and long-term relief.
Ciocon et al (107) Evaluation of elderly patients	30 patients with various degrees of degenerative lumbar canal stenosis treated with caudal epidural steroid injections. Mean age: 76 ± 6.7 yrs	A total of 3 caudal epidural steroid injections of 0.5% lidocaine with 80 mg of methylprednisolone administered at weekly intervals	Timing: initial and at 2-month intervals up to 10 months. Outcome measures: the Roland 5-point pain rating scale. Pain reduction and walking capability.	The results showed significant pain reduction for up to 10 months, with satisfactory relief in 90% of the patients.	Positive short-term and long-term relief.

and multiple other observational trials (132-161).

Of the 16 studies, 8 studies were excluded and only 8 met inclusion criteria. One study (112) was excluded as they studied effects of subarachnoid and epidural midazolam. Two studies (118, 119) studied diabetic polyneuropathy and intractable post herpetic neuralgia. One study (123) evaluated only inpatients, whereas 3 evaluations (113, 114, 120) failed to evaluate long-term relief, and finally, one study (121) was not included due to lack of data for review. Table 6 illustrates various characteristics and results of published randomized or double blind trials meeting inclusion criteria. Of the 8 non-randomized prospective trials, only 3 trials (124-126) met criteria for inclusion, whereas the remaining 5 studies (127-131) were eliminated due to multiple issues.

Of the 8 randomized trials included in evaluation, 6 were positive for short-term relief (108, 111, 115-117, 122), whereas only 3 were positive for long-term relief (111, 117, 122). Numerous non-randomized trials, both prospective and retrospective, reported good results in 18% to 90% of patients receiving cervical or lumbar interlaminar epidural steroid injections, however, without specific follow-up period. Among the 3 prospective trials included for evaluation (124-126), only one was positive (125), one was indeterminate (124), and one was negative (126).

Of the 2 randomized trials, which were positive, Dilke et al (111) studied low

back pain and sciatica, whereas Catanegra (117) studied chronic cervical radicular pain. Cuckler et al (110) also included post lumbar laminectomy syndrome patients with overall negative results. Due to a multitude of randomized trials and availability of double blind or randomized, and non-randomized prospective trials in managing lumbar radicular pain, evidence from retrospective trials was not included. However, due to only one randomized trial (117) and one prospective study (122), in managing cervical radicular pain, multiple retrospective trials (132-144) were included for review. Retrospective reports were also considered in managing chronic low back pain with or without radiculopathy (145-161).

Some studies evaluated the effectiveness of cervical epidural steroid injections in patients not only with cervical radicular pain, but also other cervical pain problems (134, 137, 140, 142). One study (138) studied patients with cervical radiculopathy. All these retrospective studies show that there is probable benefit in a significant number of patients in short-term, however the benefits appear to be limited in long-term. The results for chronic low back pain also showed positive results in short-term and negative results in long-term in chronic low back pain.

#### Transforaminal Epidural Injections

Multiple reports evaluating the effectiveness of transforaminal epidural injections included 7 randomized trials (120, 162-167); 8 prospective evaluations (124,

168-174); one prospective evaluation of change in size and pattern of disc herniation (175); and multiple retrospective reports (105, 176-187).

Among the 7 randomized controlled trials, only 3 trials (120, 162, 164) met criteria for inclusion. The trial by Kolsi et al (166) was not included since the measurements were only of short-term duration. Devulder et al (165) evaluated the effectiveness of transforaminal epidurals in post laminectomy syndrome. Karpinen et al (163, 164) used two publications to report the results of one trial. Buttermann (167) presented preliminary results at a scientific meeting in 1999 without subsequent publication. Details of the randomized trials examining the effectiveness of transforaminal epidural steroid injections in the management of spinal pain are illustrated in Table 7. All 3 studies showed effectiveness of transforaminal epidural steroids in managing nerve root pain. One study (164) showed ineffectiveness of transforaminal epidurals for disc extrusions.

Among the prospective evaluations, 3 investigations, those of Vad et al (169), Lutz et al (168), and Bush and Hillier (124) met inclusion criteria. Others were excluded because some were performed under CT, long-term results were not evaluated in some, and in others, multiple injections were performed in a short period of time. As shown in Table 8, all 3 prospective trials (124, 168, 169) were positive for short-term and long-term relief. Among the retrospective evaluations, 4 studies by Weiner and Fraser

Table 6. Characteristics of published randomized trials of interlaminar epidural injections

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/Conclusion
Carette et al (108) Randomized double blind trial	158 patients with sciatica due to a herniated nucleus pulposus. 78 patients in the treatment group. 80 patients in the placebo group. 50% of the patients had L4/5 disc herniation and 46% of the patients had L5/S1 disc herniation.	Experimental group: methylprednisolone acetate (80 mg and 8 mL of isotonic saline) Control group: isotonic saline 1 mL Frequency: 3 epidural injections 3 weeks apart	Timing: 6 weeks, 3 months, 12 months Outcome measures: Need for surgery Oswestry Disability scores	After 6 weeks, a significant difference was seen with improvement in leg pain in the methylprednisolone group. After 3 months, there were no significant differences between groups. At 12 months, the cumulative probability of back surgery was equal in both groups.	Positive short-term Negative long-term relief
Snoek et al (109) Randomized trial	51 patients with lumbar root compression documented by neurological deficit and a concordant abnormality noted on myelography. 27 patients in experimental group 24 patients in control group	Experimental group: 80 mg of methylprednisolone (2 mL) Control group: 2 mL of normal saline Frequency: single injection	Timing: 3 days and an average of 14 months Outcome measures: Pain, sciatic nerve stretch tolerance, subjective improvement, surgical treatment.	No statistically significant differences were noted in either group with regards to low back pain, sciatic nerve stretch tolerance, subjective improvement, and surgical treatment.	Negative short-term and long-term relief
Cuckler et al (110) Randomized double blind trial	73 patients with back pain due to either acute herniated nucleus pulposus or spinal stenosis. Duration: greater than 6 months. Experimental group = 42 patients, control group = 31 patients	Experimental group: 80 mg (2 mL) of methylprednisolone + 5 mL of procaine 1% Control group: 2 mL saline + 5 mL of procaine 1%	Timing: 24 hours and an average of 20 months Outcome measures: subjective improvement. Need for surgery.	There was no significant short-term or long-term improvement among both groups.	Negative short-term and long-term relief
Dilke et al (111) Randomized trial	100 patients with low back pain and sciatica of 1 week to more than 2 yrs. 51 patients in experimental group 48 patients in control group	Experimental group: 10 mL of saline + 80 mg of methylprednisolone Control group: 1 mL of saline Frequency: up to 2 injections separated by 1 week All patients received physical therapy with hydrotherapy and exercise	Timing: 2 weeks and 3 months Outcome measures: time of bedrest, days of hospitalization, pain relief, consumption of analgesics and resumption of work 3 months later	60% of the patients in the treatment group and 31% of the patients in the control group improved immediately after the injections. A greater proportion of actively treated patients had no pain at 3 months, took no analgesics, resumed work and fewer of them underwent subsequent surgery or other non-surgical treatment.	Positive short-term and long-term relief
Ridley et al (115) Randomized trial	35 patients with low back pain and sciatica of mean duration approximately 8 months 19 patients in experimental group 16 patients in control group	Experimental group: 10 mL of saline + 80 mg of methylprednisolone (n=19) Control group: saline 2 mL, interspinous ligament (n=16)	Timing: 1 weeks, 2 weeks, 3 months and 6 months Outcome measures: pain control improvement in straight leg raising	90% of the patients in the treated group compared to 19% in the control group showed improvement at 1 week, 2 weeks and 12 weeks. By 24 weeks, the relief deteriorated to pre-treatment levels	Positive short-term relief Negative long-term relief
Rogers et al (116) Randomized single blind sequential analysis	30 patients with low back pain 15 patients in experimental group 15 patients in control group	Experimental group: local anesthetic + steroid Control group: local anesthetic alone	Timing: 1 month Outcome measures: pain relief Nerve root tension signs	Lumbar epidural injection of steroid together with local anesthetic produced significantly better results. Long-term results were similar for both.	Positive short-term relief Negative long-term relief
Catanegra et al (117) Randomized trial with cervical interlaminar epidural steroid injections	24 patients with chronic cervical radicular pain, however without need of surgery, but suffering for more than 12 months i. 14 patients receiving local anesthetic and steroid ii. 10 patients receiving local anesthetic, steroid + morphine sulfate	i. 0.5% lidocaine + triamcinolone acetanide ii. Local anesthetic + steroid + 2.5 mg of morphine sulfate	Timing: 1 month, 3 months, and 12 months 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 months, 6 months, and 12 months.	Positive short-term and long-term relief

Table 6. Characteristics of published randomized trials of interlaminar epidural injections (Continued)

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/Conclusion
Stav et al (122) Randomized trial of cervical epidural steroid injections	52 patients with chronic, resistant cervical brachialgia 25 patients in experimental group 17 patients in control group	Experimental group: cervical epidural steroid and lidocaine injections Control group: steroid and lidocaine injections into the posterior neck muscles Frequency: 1 to 3 injections were administered at 2 weeks intervals, based on the clinical response All patients continued pre-study treatment with drugs and physiotherapy	Timing: 1 week and 1 year Outcome measures: pain relief, change in deep tendon reflexes or sensory loss, change in range of motion Reduction of daily dose of analgesics Return to work	After 1 week, 76% of the patients in cervical epidural group compared to 36% of the patients in the neck injection group showed improvement. At 1 year, 68% of the cervical epidural group continued to have relief compared to 12% of the control group.	Positive short-term and long-term relief

Table 7. Details of randomized trials studying the effectiveness of transforaminal epidural steroid injections for low back pain

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/Conclusion
Riew et al (162) Randomized double blind trial	55 patients with lumbar disc herniations or spinal stenosis referred for surgical evaluation. All subjects had clinical indications for surgery, and radiographic confirmation of nerve root compression. All patients had failed a minimum of 6 weeks of conservative care or had unrelenting pain. 28 patients in experimental group (71%) 27 patients in control group (33%)	Experimental group: transforaminal nerve root or epidural steroid injection with 1 mL of 0.25% bupivacaine and 6 mg of betamethasone Control group: 1 mL of 0.25% bupivacaine. The patient was allowed to choose to receive as many as 4 injections at any time during the follow-up.	Timing: 1 year Outcome measures: Injections were considered to have failed if the patient opted for operative treatment. Multiple injection therapy was not considered as failure. North American Spine Society questionnaire.	Of the 28 patients in the experimental group with bupivacaine and betamethasone, 20 decided not to have the operation. Of the 27 patients in the control group receiving bupivacaine alone, 9 elected not to have the operation. They had highly significant pain relief and functional improvement.	Positive short-term and long-term relief.
Kraemer et al (120) Randomized double blind study	49 patients with lumbar radicular symptoms with 24 patients in the steroid group and 25 patients in the normal saline group.	Experimental group: transforaminal epidural with local anesthetic and 10 mg of triamcinolone. Control group: local anesthetic only. Normal saline group received IM steroid injections to avoid the systemic steroid effect.	Timing: not mentioned Outcome measures: Pain relief	Single-short epidural perineural injection was effective in the treatment of lumbar radicular pain.	Positive short-term and long-term relief.
Karppinen et al (163, 164) Randomized double blind trial	160 consecutive, eligible patients with sciatica with unilateral symptoms of 1 to 6 months duration. None of the patients have undergone surgery.	Experimental group: local anesthetic and methylprednisolone Control group: normal saline	Timing: 2 weeks, 3 months, 6 months Outcome measures: Pain relief, sick leaves, medical costs, and future surgery Nottingham Health Profile	In the case of contained herniations, the steroid injection produced significant treatment effects and short-term in leg pain, straight leg raising, disability and in Nottingham Health Profile, emotional reactions and cost effectiveness.	Positive short-term and long-term relief.



Table 8. Details and results of non-randomized trials of transforaminal epidural injections

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/Conclusion
Vad et al (169) A prospective study randomized by patient choice from the private practice of a single physician.	Patients with leg pain, older than 18 years, had been symptomatic longer than 6 weeks, had undergone a lumbar spine magnetic resonance imaging scan documenting herniated nucleus pulposus or manifested clinical signs such as radicular pain and sensory or fixed motor deficits consistent with lumbar radiculopathy.	Experimental group: transforaminal epidural steroid injection. 1.5 mL each of betamethasone acetate, 9 mg and 2% preservative-free Xylocaine per level. Control group: trigger point injections. All patients received a self-directed home lumbar stabilization program consisting of four simple exercises emphasizing hip and hamstring flexibility and abdominal and lumbar paraspinal strengthening.	Timing: 3 weeks, 6 weeks, 3 months, 6 months, and 12 months. Outcome measures: Roland-Morris score, visual numeric score, finger-to-floor distance, patient satisfaction score.	Fluoroscopically guided transforaminal epidural steroid injections yielded better results compared to saline trigger point injections. The group receiving transforaminal epidural steroid injections had a success rate of 84%, as compared with the 48% for the group receiving trigger point injections.	Positive short-term and long-term relief
Lutz et al (168) A prospective case series.	69 patients with lumbar herniated nucleus pulposus and radiculopathy. 69 patients were recruited. Every patient in the case series had documented magnetic resonance imaging findings that showed disc herniation with nerve root compression.	Transforaminal epidural steroid injections with 1.5 cc of 2% Xylocaine and 9 mg of betamethasone acetate.	Timing: 28 to 144 weeks Outcome measures: At least $\pm 50\%$ reduction in pre-injection and post-injection visual numerical pain scores.	A successful outcome was reported by 52 of the 69 patients (75.4%) at an average follow-up of 80 weeks (range 28-144 weeks).	Positive short-term and long-term relief
Bush and Hillier (124) Prospective evaluation of cervical interlaminar and transforaminal epidural injections	68 patients with neck pain and cervical radiculopathy.	Following the first blind cervical epidural injection, if a significant improvement was not seen, a repeat injection was performed trans foraminally with fluoroscopy guidance within 1 month. A third injection was also performed if needed in the same manner as the second injection.	Timing: 1 month to 1 year Outcome measures: Pain relief	93% of the patients were reported to have good pain relief lasting for 7 months.	Positive short-term and long-term relief
Weiner and Fraser (183) A retrospective evaluation	30 patients with lateral foraminal or extraforaminal herniation of a lumbar disc were evaluated with foraminal injection of local anesthetic and steroids for radiculopathy	Transforaminal injection of 2 mL of 1% lidocaine combined with 11.4 mg of injectable betamethasone.	Timing: 1 to 10 years Outcome measures: Pain scale: Use of analgesics, work status, recreational activities.	22 had lasting relief of their symptoms. 14 had no pain allowing them to participate freely in their usual activities. Of the 17 patients at work, 13 had returned to the same job.	Positive short-term and long-term relief
Manchikanti et al (105) Compared the 3 routes of epidural steroid injections in the management of low back in retrospective manner	225 patients randomly derived from a total sample of 624 patients suffering with low back pain from a total of 972 patients referred for pain management were evaluated.	Group I: interlaminar epidurals with a midline approach without fluoroscopy. Group II: caudal epidurals under fluoroscopy. Group III: transforaminal epidural steroid injections.	Timing: 1, 3, 6, 12 months Outcome measures: Pain relief	Group III reported $\pm 50\%$ relief per procedure of $7.69 \pm 1.20$ weeks, which was superior to blind interlaminar epidurals.	Positive short-term and long-term relief
Rosenberg et al (186) Retrospective evaluation	92 patients with radiculopathic back pain due to spinal stenosis, herniated discs, spondylolisthesis, and degenerative discs.	Group I: Previous back surgery (16%) Group II: Discogenic abnormalities: herniations, bulges or degeneration (42%) Group III: spinal stenosis (32%) Group IV: those without MRI (11%)	Timing: 2, 6 and 12 months Outcome measures: Pain relief	The pain scores for all patients improved significantly at all three points. Greater than 50% improvement after one year was seen in 23% of Group I; 59% in Group II; 35% in Group III and 67% in Group IV.	Positive short-term and long-term relief
Wang et al (187) Retrospective evaluation	69 patients with lumbar herniated discs	All patients were treated with 1-6 epidural steroid injections	Timing: NA Outcome measures: Pain relief Avoidance of surgeon	77% of patients had significant improvement and refused surgery	Positive short-term and long-term relief

(183), Rosenberg et al (186), Wang et al (187) and Manchikanti et al (105) met inclusion criteria. All retrospective evaluations showed positive short-term and long-term relief.

### Complications and Side Effects

The most common and worrisome complications and side effects of caudal, interlaminar, and transforaminal epidural injections are of two 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 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 (188-239). No major complications or side effects were reported in the trials presented in the review.

### DISCUSSION

This systematic review evaluated the effectiveness of epidural injections in patients with chronic spinal pain. The evidence was evaluated for 3 types of epidurals separately.

For the transforaminal epidural injections, three (120, 162, 164) of the 7 randomized trials (120, 162-167), showed positive short-term and long-term effectiveness for lumbar nerve root pain. Three prospective evaluations (124, 168, 169) showed positive short and long-term results. Four retrospective evaluations (105, 183, 186, 187) were included which showed positive results overall. Multiple randomized and non-randomized trials of transforaminal epidural injections provided strong evidence for short-term and long-term relief in managing lumbar nerve root pain. Their effectiveness in post lumbar laminectomy syndrome and disc extrusions is inconclusive. There is no published evidence of effectiveness of transforaminal epidural injections in chronic neck or chronic low back pain, post cervical or laminectomy syndrome, and cervical or thoracic radicular pain.

The combined overall evidence of caudal epidural steroid injections, based on randomized trials and nonrandomized trials (prospective and retrospective trials) is strong for short-term relief and moderate for long-term relief with two (92, 93)

of three (92-94) randomized trials, and 4 of 4 non-randomized trials (102-104-106) demonstrating positive results in radicular pain. However, the evidence for chronic low back pain and spinal stenosis appears to be limited as there are no randomized or double-blind trials evaluating this effect. Non-randomized trials (100, 101, 105, 107) all showed positive results in chronic low back pain after the facet joint pain was excluded (100, 101, 105), and also in spinal stenosis (107).

For interlaminar epidural injections, of the 8 randomized trials included, 6 trials (108, 111, 115-117, 122) showed positive evidence for short-term relief, and 3 of 8 (111, 117, 122) showed positive evidence for long-term relief. The overall effectiveness of interlaminar epidural steroid injections in managing chronic spinal pain is moderate for short-term relief and limited for long-term relief in managing lumbar radicular pain. However, there was no significant evidence based on randomized trials of effectiveness of interlaminar epidural steroids in managing cervical radicular pain. Further analysis combining one randomized trial, one prospective trial and multiple retrospective evaluations (132-144), demonstrated moderate evidence for short-term, and limited evidence for long-term relief. The limited evidence for management of chronic low back pain without radiculopathy was based on all the retrospective studies.

The first systematic review of effectiveness of epidural steroid injections was performed by Kepes and Duncalf in 1985 (59). They concluded that the rationale for epidural and systemic steroids was not proven. However, in 1986 Benzon (60), 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 (59) and Benzon (60) may have been due to the fact that Kepes and Duncalf (59) included studies on systemic steroids whereas Benzon (60) limited his 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 (57). In this report, Bogduk et al (57) extensively studied cau-

dal, 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 (61) updated his 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 (62) reviewed 12 trials of lumbar and caudal epidural steroid injections and reported positive results from only six 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 five studies involving caudal epidural steroid injections were positive, whereas 5 of 7 studies were negative for lumbar epidural steroid injections. Koes et al (63) updated their review of epidural steroid injections for low back pain and sciatica, including three more studies with a total of 15 trials which met the inclusion criteria. In this study, they concluded that of the 15 trials, eight reported positive results of epidural steroid injections. Both reviews mostly reflected the quality of studies, rather than any meaningful conclusion.

Nelemans et al's (66) 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 (70), 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. Rozenburg et al (70) 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 (71) 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. Many of these deficiencies were noted in our review also, in spite of the fact that we have included non-randomized trials.

With respect to complications and side effects, only transient minor complaints were reported in the trials presented in this review. However, potential complications also have been described. Spinal cord trauma and spinal cord or epidural hematoma formation are catastrophic complications. One of the suggestions has been to perform interventional procedures only in an awake patient and in the cervical spine by limiting the midline injection to be performed only at C7/T1 except in rare circumstances. However, it has also been reported that even an awake patient may not be able to detect spinal cord puncture (241). Thus, the recommendation to limit the midline injection only at C7/T1 is based neither on consistent clinical nor anatomical evidence. Three cases of paraplegia were reported after lumbosacral nerve root block in post lumbar laminectomy patients (229). In each patient, paraplegia was reported suddenly. In each patient after injection of a steroid solution, post procedure magnetic resonance imaging (MRI) revealed spinal cord edema in the low thoracic region. The authors postulated that in these patients, the spinal needle penetrated or injured an abnormally low dominant radiculomedullary artery, a recognized anatomical variant. This vessel, also known as artery of Adamkiewicz, in 85% of individuals arises between T9 and L2, usually from the left, but in a minority of people, may arise from the lower lumbar spine and rarely even from as low as S1 (229). Others also have reported similar complications (234-236). Side effects related to the administration of steroids are gener-

ally 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. One study (228) showed no significant difference in patients undergoing various types of interventional techniques with or without steroids. Further, it has also been shown that the most commonly used steroids in the epidural steroids in the United States, methylprednisolone acetate, triamcinolone acetate, and betamethasone acetate, and phosphate mixture have all been shown to be safe at epidural therapeutic doses in both clinical and experimental studies (242-250).

#### CONCLUSION

This systematic review, which included not only randomized trials, but also all available non-randomized trials, showed variable effectiveness of epidural injections. Strong evidence was provided for transforaminal epidural steroid injections in managing lumbar nerve root pain. Moderate evidence was provided for caudal epidural steroid injections in managing lumbar radicular pain. Evidence for other conditions was either limited or inconclusive.

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