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A Systematic Review

Role of Epidural Steroids in the Management of Chronic Spinal Pain: A Systematic Review of Effectiveness and Complications

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Background: Epidural steroid injections are commonly used for chronic spinal pain. However, there is no conclusive evidence regarding their effectiveness, and debate continues as to their value in managing chronic spinal pain.

Objective: To evaluate various types of epidural injections (interlaminar, transforaminal, and caudal) for managing chronic spinal pain (axial and radicular).

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 the Cochrane Musculoskeletal Review Group for randomized trials.

Methods: Data sources included relevant English literature identified through searches of MEDLINE and EMBASE (January 1966 to November 2004), 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 for trials with different control groups, with different modes of epidurals (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 was pain relief. Other outcome measures were functional improvement, improvement of psychological status, and return to work. Short-term improvement was defined as less than 6 weeks, and long-term improvement was defined as 6 weeks or longer.

Results: For 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. For cervical radicular pain with cervical interlaminar epidural steroid injections, the evidence was moderate.

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

The evidence for caudal epidural steroid injections was strong for short-term relief and moderate for long-term relief. For managing chronic postlumbar laminectomy syndrome and spinal stenosis the evidence was limited for low back and radicular pain. The evidence was moderate for chronic low back pain.

Conclusion: The evidence for effectiveness of epidural injections in managing chronic spinal pain ranged from limited to strong.

Keywords: Spinal pain, low back pain, epidural steroids, interlaminar, caudal, transforaminal, radiculopathy, axial pain, spinal stenosis

Among chronic pain syndromes, pain emanating from various structures of the spine constitutes the majority of the problems. The lifetime prevalence of spinal pain was reported as 65% to 80% (1-8). Studies of prevalence of low back and neck pain and economic impact and its impact on general health (4-18) showed significant disability in all ages of the population with the elderly suffering not only with pain of longer duration, but with a higher frequency; musculoskeletal symptoms for multiple body parts (2 or more) were more prevalent (64% of all workers) than those for single body regions (19%); and chronic persistent back pain and neck pain in children and adults is seen in up to 60% of patients, as long as 5 years or longer after the initial episode.

Epidural injections with or without corticosteroids is one of the commonly used interventions in managing chronic spinal pain (1, 19). However, the use of epidural steroid injections is still debated. Several approaches are available to access the lumbar epidural space: interlaminar, transforaminal, and caudal (1, 20-23). There are substantial differences between the three approaches. The interlaminar entry is directed more closely to the assumed site of pathology requiring less volume than the caudal route. The transforaminal approach is target specific using the smallest volume in fulfilling the aim of reaching the primary site of pathology; namely the ventrolateral space. In contrast, the caudal entry is relatively easily achieved with minimal risk of inadvertent dural puncture, but requiring high volumes of injectate to reach target structures. Due to inherent variations, differences, advantages, and disadvantages applicable to each technique (including effectiveness and outcomes), interlaminar epidural injections (cervical, thoracic and lumbar epidural injections) transforaminal epidural injections (cervical, thoracic and lumbosacral), and caudal epidural injections are considered as separate entities

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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 one 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, two 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 one 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 1

within epidural injections. As such, they should be discussed individually.

The 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. 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 (24-37), even though an inflammatory basis for either axial or radicular pain has not been proven (32, 38, 39).

This systematic review was undertaken due to conflicting opinions and inconclusive evidence in the literature (1, 20, 23, 40-47). Further, authors of this review strongly believe that due to the inherent variations and differences in the 3 techniques applied in the delivery of epidural steroids, most of the previous reviews were not only incomplete, but also inaccurate. Thus, due to variations, differences, advantages, and disadvantages applicable to each technique, interlaminar epidural injections, transforaminal epidural injections, and caudal epidural injections are considered as separate entities.

Methods

Literature Search

Our literature search included MEDLINE and EMBASE (Jan 1966 – Nov 2004), 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, published in the English language. The search strategy consisted of diagnostic interventional techniques, epidural injections and steroids, interlaminar epidurals, 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, and reports of complications. 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 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 (48), as shown in Appendix A to D. For evaluation of randomized trials, criteria described by Cochrane Review Group for musculoskeletal disorders (49) also have been utilized (Appendix E).

For studies to be included, an algorithmic criteria should have been met (Appendix F) and a study should answer positive questions (at least partially) in all three categories (1, 50).

Data Extraction

Study evaluation and inclusion and exclusion is shown in Appendix F. Methodologic quality assessment was performed as described in the Appendices.

Analysis of Evidence

Qualitative analysis was conducted, using five levels of evidence for effectiveness of epidural steroids as illustrated in Table 1. Pain relief was evaluated on both a short-term (less than 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 concluded that it was effective in observational studies. All other conclusions were considered negative. If, in the opinion of the reviewers, there was conflict with the conclusion, appropriate explanations were provided.

Results

Interlaminar Epidural Injections

Our search strategy yielded a total of 236 articles. Relevant studies evaluating the effectiveness of interlaminar epidural injections, specifically lumbar epidural injections included 19 randomized or double blind trials (51-69), 8 non-randomized prospective trials (68-77), and multi-

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
Carette et al (65) Randomized double blind trial AHRQ Score 10/10 Cochrane Score 10/10	158 patients with sciatica due to a herniated nucleus pulposus. Treatment group: 78 Placebo group: 80	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 and 12 months, there were no significant differences between groups.	Positive short-term and negative long-term
Snoek et al (66) Randomized trial AHRQ Score 7/10 Cochrane Score 6/10	51 patients with lumbar root compression documented by neurological deficit and a concordant abnormality noted on myelography. Experimental group : 27 Control group : 24	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
Cuckler et al (51) Randomized double blind trial AHRQ Score - 9/10 Cochrane Score 9/10	73 patients with back pain due to either acute herniated nucleus pulposus or spinal stenosis of > 6 months. Experimental group = 42 Control group = 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 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
Dilke et al (52) Randomized trial AHRQ Score 7/10 Cochrane Score 7/10	100 patients with low back pain and sciatica of 1 week to more than 2 yrs. Experimental group: 51 Control group: 48	Experimental group: 10 mL of saline + 80 mg of methylprednisolone. Control group: 1 mL of saline .	Timing: 2 weeks and 3 months Outcome measures: pain relief, consumption of analgesics and resumption of work	Initial Improvement: 60% in the treatment group and 31% in the control group. A greater proportion of actively treated patients improved at 3 months.	Positive short-term and long-term
Ridley et al (56) Randomized trial AHRQ Score 9/10 Cochrane Score 8/10	35 patients with low back pain and sciatica of mean duration approximately 8 months. Experimental group =19 Control group =16	Experimental group: 10 mL of saline + 80 mg of methylprednisolone (n=19). Control group: saline 2 mL, interspinous ligament (n=16).	Timing: 1 week, 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 and negative long-term
Rogers et al (57) Randomized single blind sequential analysis AHRQ Score-6/10 Cochrane Score 5/10	30 patients with low back pain. Experimental group =15 Control group =15	Experimental group: local anesthetic + steroid. Control group: local anesthetic alone.	Timing: 1 month Outcome measures: pain relief and nerve root tension signs	Experimental group significantly better results. Long-term results were similar for both.	Positive short-term relief and negative long-term
Kraemer et al (61) Randomized trial AHRQ score: 6/10 Cochrane score: 5/10	Control = 46 Intervention=40	Control :paravertebral local injection of local anesthetic, with intramusclar steroid injection. Intervention group : lumbar interlaminar steroid injection.	Timing: 3 weeks, and 3 months Pain relief	Epidural injections were more effective than paravertebral injections. Epidural perineural injections were more effective than conventional posterior epidural injections.	Positive short-term and negative long-term
Pirbudak et al (68) Randomized non blinded AHRQ score: 7/9 Cochrane score: 6/10	92 patients with sciatica. Experimental with steroids and amitriptyline = 46 Control with steroids=46	Experimental:benzylprednisolone (14 mg) + bupivacaine and 10-50 mg oral amitryptiline. Control; benzylprednisolone and bupivacaine.	Timing: 2 weeks, 6 weeks and 9 months. Outcome measures: VAS and Oswestry low back pain disability questionnaire	Lumbar epidural steroid injection reported pain relief up to 6 months. Additional oral amitryptiline increased pain relief to 9 months.	Positive short-term and long-term
McGregor et al (69) AHRQ Score 6/10 Cochrane score: 5/10	44 patients with low back and leg pain	Caudal epidural vs lumbar epidural.	Visual analog scale	There were no significant differences between the techniques.	Negative short term and long term

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 (58) Randomized trial with cervical interlaminar epidural steroid injections AHRQ Score - 7/10 Cochrane Score 6/10	14- local anesthetic and steroid 10 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 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
Stav et al (63) Randomized trial of cervical epidural steroid injections AHRQ Score - 6/10 Cochrane Score - 5/10	Experimental =25 Control=17	Experimental group: cervical epidural steroid and lidocaine injections Control group: steroid and lidocaine injections into the posterior neck muscles	Timing: one week and one 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

ple other observational trials (78-106).

Methodological Criteria

Of the randomized trials, 11 studies met inclusion criteria (51, 52, 56-58, 61, 63-65, 68, 69). One study (53) was excluded as they studied effects of subarachnoid and epidural midazolam. Two studies (59, 60) focused on diabetic polyneuropathy and intractable post herpetic neuralgia. One study (64) evaluated only inpatients, whereas 4 evaluations (54, 55, 61, 67) failed to evaluate long-term relief, and, finally, one study (62) was not included due to lack of data for review. Tables 2 & 3 illustrate various characteristics and results of published randomized trials meeting inclusion criteria.

Of the 9 non-randomized prospective trials, only 3 studies (70-78) met the criteria for inclusion.

Effectiveness

Of the 9 randomized trials (51, 52, 56, 57, 65-69) included in the evaluation of lumbar radiculitis, 5 were positive for short-term relief (52, 56-58, 65), whereas only one study was positive for long-term relief (52). Among the 3 prospective evaluations included for evaluating low back and lower extremity pain (71, 72, 74), two studies were positive for short-term relief (71, 74) whereas one was positive for long-term relief (71)

Among the other prospective evaluations, a study evaluating management of lumbar radiculopathy (72), a study evaluating effect in spinal stenosis (75), another study evaluating and comparing single caudal injection with interlaminar injection (69), and another study evaluating correlation of epidural steroid injection as a predictor of surgical outcome (77), were all shown to be negative.

In the evaluation of cervical pain and radiculopathy, two randomized trials (58, 63), one prospective evaluation (70), and multiple retrospective evaluations were available (78-89). Both the randomized trials (58, 63) evaluating the effectiveness of interlaminar cervical epidural steroids in managing cervical radiculopathy were positive. The single prospective evaluation of the cervical spine (70) was not included as all the patients who underwent interlaminar epidural steroid injections also underwent transforaminal epidural steroid injections.

Of the 3 randomized trials, which were positive, Dilke et al (52) studied low back pain and sciatica, whereas Castagnera et al (58) and Stav et al (63) studied chronic cervical radicular pain. Cuckler et al (51) also included post lumbar laminectomy syndrome patients with overall negative results. Due to a multitude of randomized trials and the availability of double blind or randomized, and prospective trials, evidence from retrospective trials was not included.

Level of Evidence

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 inconclusive in the management of axial neck pain, axial low back pain, and lumbar spinal stenosis with lumbar or cervical interlaminar epidural steroid injections.

Transforaminal Epidural Injections

Our search strategy yielded a total of 189 publications. Relevant reports evaluating the effectiveness of transforaminal epidural injections included 8 randomized trials (61, 107-113), 14 prospective evaluations (70, 114-126), and multiple retrospective reports (127-141). Table 4 shows study characteristics of randomized trials evaluating transforaminal epidural steroid injections, along with methodological criteria, whereas, Table 5 shows descriptions of non-randomized studies.

Description of Study Characteristics

All the randomized evaluations studied the effect of transforaminal epidural steroid injections in lumbar radiculitis with disc herniation except Devulder et al (110), studying the effectiveness of transforaminal epidural steroid injections in post lumbar laminectomy syndrome.

Riew et al (107) evaluated transforaminal epidural steroid injections and local anesthetic injections in patients with either a disc herniation or central or lateral stenosis. They studied the number of patients avoiding surgical intervention. Karppinen et al (108, 109) evaluated transforaminal epidural steroid injec-

tions, in patients with MRI-confirmed herniated nucleus pulposus. The outcome measures were 50% relief of leg pain and cost effectiveness. Vad et al (112) 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 (113) evaluated the effectiveness of transforaminal epidural and compared it with interspinous corticosteroid injection. Devulder et al (110) 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%.

Methodological Criteria

Among the 8 randomized controlled trials, only 5 trials (107, 109, 110, 112, 113) met the criteria for inclusion (Table 4). The trial by Kolsi et al (111) was not included since the measurements were only of short-term duration. Karppinen et al (108, 109) used two publications to report the results of one trial. Kraemer et al (61) described lumbar epidural perineural injection, however, using an interlaminar approach, a non-validated technique.

Among the 14 prospective evaluations (70, 114-126), 6 were included (70, 114, 121-123, 126). Characteristics of the observational studies are described in Table 4.

Effectiveness

Among the 5 randomized trials included in the evidence synthesis meeting inclusion criteria (Table 3), 4 of them evaluated the effectiveness of lumbar disc herniation and radiculopathy (107, 109, 112, 113), whereas, one study (110) evaluated the response in post lumbar laminectomy syndrome. Three of the four studies showed positive results with short-term and long-term improvement. The study in postlumbar laminectomy syndrome was negative.

Among the 6 prospective evaluations included in the study, 2 studies evaluated the effectiveness of cervical transforaminal epidurals (70, 123), showing positive results. The remaining 4 prospective studies included patients with low back and lower extremity pain. One study also evaluated lumbar disc herniation regression after successful epidural steroid injection (120). A second study (122) compared effectiveness of transforaminal epidural steroid injections in the lumbar spine with discectomy. All the prospective evaluations showed positive short-term and long-term results. Multiple retrospective evaluations also showed positive results. Due to the significant number of publications available in the English literature with randomized and prospective designs, retrospective evaluations were not included in the evidence synthesis.

Level of Evidence

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

Caudal Epidural Injections

Our search strategy yielded a total of 232 articles. Relevant reports studying caudal epidural injections included 9 randomized (142-149), 5 prospective evaluations (69, 150-153, 156), and multiple retrospective evaluations (1, 154, 155). The results of published reports of the randomized trials are described in Table 6, while Table 7 shows descriptions of prospective evaluations.

Methodological Quality

Of the 9 randomized trials, 2 trials were excluded. One study (146) was excluded due to non-availability of analyzable information, whereas a second trial (145) was excluded due to lack of long-term data.

Of the 7 randomized trials, 3 trials evaluated predominantly patients with radiculopathy or sciatica (142-144), 2 trials evaluated patients suffering with pain following failed back surgery syndrome (148, 149), and, one study (147) evaluated a mixed population with 50% post lumbar laminectomy syndrome patients. One study (69) compared blind interlaminar epidurals with caudal epidural steroid injections.

Among the 5 non-randomized evaluations (150-153, 156), radiculopathy or sciatica patients were studied in 2 evaluations (152, 153), the role of caudal epidural in chronic low back pain was studied in an additional 2 studies (150, 151), and the role of caudal epidural steroids was studied in spinal stenosis in one study (156).

Effectiveness

Of the 7 randomized trials, 4 were positive for short-term pain relief (142, 143, 147, 148), and 3 were positive for long-term relief (142, 144, 147).

Among 7 randomized trials included for analysis, of the 4 trials evaluating predominantly radiculopathy, 2 were positive (142, 143) and 2 studies were negative (69, 144) for short-term relief, whereas 2 of 3 were positive for long-term relief (142, 144). Of the two studies with postlumbar laminectomy syndrome (148, 149), only one study (148) was positive for short-term. One study (147) 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 prospective studies, 2 studies evaluating radiculopathy or sciatica (152, 153), and 2 studies evaluating the effectiveness of caudal epidural steroid injections in chronic low back pain (150, 151), were positive, and one study evaluating the effectiveness of caudal in lumbar spinal stenosis was positive.

Level of Evidence

Overall, 3 of the 5 randomized trials were positive for pain of radiculopathy, and 2 of 3 were positive for post lumbar laminectomy syndrome among randomized trials.

Among the prospective evaluations, 4 of the 5 studies evaluating radicular pain or low back pain were positive.

Thus, positive long-term relief trials was 60% for radiculopathy or sciatica and 67% for post lumbar laminectomy syndrome. Among the prospective evaluations, 80% were positive for radiculopathy and chronic low back pain.

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 post lumbar

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 wk
Riew et al (107) Randomized double blind trial AHRQ Score 8/10 Cochrane Score 7/10	55 patients with lumbar disc herniations or spinal stenosis referred for surgical evaluation. All pts. had failed a minimum of 6 weeks of conservative care or had unrelenting pain. 28 patients in experimental group 27 patients in control group	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. 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
Karppinen et al (108, 109) Randomized double blind trial AHRQ Score 9/10 Cochrane Score 8/10	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 leave, 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.	Negative short-term and long-term
Vad et al (112) A prospective study randomized by patient choice from the private practice of a single physician. AHRQ Score 7/10 Cochrane Score 7/10	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 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
Devulder (110) AHRQ Score 6/10 Cochrane Score 5/10	An open, nonblinded, randomized study on 60 patients with documented fibrosis in fewer than three nerve roots.	Group A =20 patients were injected with 1 ml bupivacaine 0.5% combined with 1500 units hyaluronidase and 1 ml saline per nerve root sleeve Group B= 20 were treated with 1 ml bupivacaine 0.5% combined with 40 mg methylprednisolone solution (Depo Medrol) per nerve root Group C; was treated with bupivacaine 0.5% combined with 1500 units hyaluronidase and 40 mg methylprednisolone solution. The volume of each injection was 2 ml. and were given twice at an interval of 1 wkeek.	The patients were evaluated on a verbal pain rating scale 1, 3, and 6 months 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 three treatment groups (after 1 month, $p = 0.71$; after 3 months, $p = 0.69$; after 6 months, $p = 0.66$. The Friedman test showed a significant decrease in treatment score as a function of time in groups B and C ($p = 0.015$) but not in group A ($p = 0.074$). Corticosteroids seem responsible for the last phenomenon.	Negative short-term and long-term
Thomas (113) AHRQ Score 6/10 Cochrane Score 5/10	Thirty-one patients (18 females, 13 males) with discal radicular pain of less than 3 months' duration	Patients 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 then at 6 months, but only by mailed questionnaire.	At day 6, the between-group difference was significantly in favor of the transforaminal group with respect to Schober's index, finger-to-floor distance, daily activities, and work and leisure activities on the Dallas pain scale. At day 30, pain relief was significantly better in the transforaminal group. At month 6, answers to the mailed questionnaire still showed significantly better results for transforaminal injection concerning pain, daily activities, work and leisure activities and anxiety and depression, with a decline in the Roland-Morris score.	Positive short-term and long-term

Table 5. *Details and results of non-randomized trials of transforaminal epidural injections*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s)
Lumbar Spine					Short-term relief <6 wks Long-term relief ≥ 6 wks
Lutz et al (114) A prospective case series. AHRQ Score 4/8	69 patients with lumbar herniated nucleus pulposus and radiculopathy were recruited. Every patient in the case series had documented MRI 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 ±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
Butterman (121) Prospective evaluation AHRQ Score 4/8	232 patients who were referred for treatment of DDD 171 patients who were possible spinal arthrodesis candidates.	Transforaminal epidural steroid injections or Intradiscal steroid injections (ISIs)	Pain and function were determined by a self-administered outcomes questionnaire that consisted of a 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, as assessed by outcomes scores at short-term follow-up. However, at 2 years, less than one-third had not had additional invasive treatment. Patients with inflammatory end-plate changes had greater improvement in the first 6 months than did those patients without the end-plate changes.	Positive short-term and long-term
Butterman (122) Prospective evaluation AHRQ Score 4/8	169 patients 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 fifty patients who had epidural steroid injection reported that the treatment had been effective. Patients who had discectomy had the most rapid decrease in symptoms, with 92% to 98% of the patients reporting that the treatment had been successful over the various follow-up periods.	Positive short-term and long-term
Botwin et al (126) Prospective evaluation AHRQ Score 4/8	34 patients who met our inclusion criteria for the treatment of unilateral radicular pain from degenerative lumbar spinal stenosis	Fluoroscopically guided lumbar transforaminal epidural injections. The injectant consisted of 12 mg of betamethasone acetate and 2 ml of 1% preservative-free lidocaine HCL.	Patients were evaluated by an independent observer and received questionnaires before the initial injection, at 2 mo, and at 12 mo after the injections. Questionnaires included a visual analog scale, Roland 5-point pain scale, standing/walking tolerance, and patient satisfaction scale.	75% of patients 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 patients had improved walking tolerance, and 57% had improved standing tolerance at 12 mo.	Positive short-term and long-term
Cervical Spine					
Bush and Hillier (70) Prospective evaluation AHRQ Score 4/8	68 patients with neck pain and cervical radiculopathy.	Transforaminal cervical epidural steroid injections	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
Cyteval (123) AHRQ Score 4/8	30 patients with cervical radiculopathy 16 patients with foraminal degenerative stenosis 14 patients with disk herniation	Percutaneous periradicular foraminal steroid infiltration under CT control	The intensity of radicular pain was scored on an analogic visual scale (AVS). Pain relief was classified as excellent when the pain had diminished by 75% or more; good, by 50%-74%; fair by 25%-49%; or poor, by less than 25%. The patients were followed up at 2 weeks and at 6 months.	Good pain relief was reported in 60% of patients. There was no rebound of pain at the 6-month follow-up.	Positive short-term and long-term

Table 6. *Characteristics of published randomized trials of caudal epidural injections*

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/ Conclusion
					Short-term relief <6 wks Long-term relief ≥ 6 wk
McGregor et al (69) AHRQ Score 6/10 Cochrane Score 5/10	44 patients with low back and leg pain	Caudal epidural vs lumbar epidural.	Visual Analog Scale	There was no significant improvement. There were no differences between both techniques	Negative short term and long term relief.
Breivik et al (142) Randomized double blind trial. Randomization according to a list of random numbers. Parallel, cohort design AHRQ Score 8/10 Cochrane Score 7/10	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 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 patients reported considerable pain relief in experimental group compared to 26% of the patients in the placebo group.	Positive short-term and long-term
Bush and Hillier (143) Randomized double blind trial. 28 patients were randomized; only 23 patients were entered into the study. AHRQ Score- 8/10 Cochrane Score 8/10	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 acetonide + 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 and negative long-term
Matthews et al (144) Double blind. Stratification by age and gender. Survival curve analyses based on cumulative totals recovered. AHRQ Score - 8/10 Cochrane Score 7/10	57 patients with sciatica with a single root compression Experimental group: male/female: 19/4, median duration of pain: 4 weeks . Control group: male/female: 24/10, median duration of pain: 4 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 and positive long-term
Helsa and Breivik (147) Double blind trial with crossover design AHRQ Score - 7/10 Cochrane Score 7/10	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 occu-rred 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
Revel et al (148) Randomized trial. AHRQ Score 7/10 Cochrane Score 6/10	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 predni-solone 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 negative long-term
Meadeb et al (149) Randomized trial. Parallel-group study. AHRQ Score 6/10 Cochrane Score 6/10	47 post lumbar laminectomy syndrome patients 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 months.	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

Table 7. *Characteristics and results of prospective studies of caudal epidural injections*

Study/Methods	Participants	Interventions	Outcomes	Results	Outcomes/ Conclusion Short-term relief <6 wks Long-term relief ≥ 6 wks
Yates (152) Prospective evaluation AHRQ Score 5/8	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 given at weekly intervals in 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
Waldman (153) Prospective evaluation with independent observer review. AHRQ Score 5/8	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, which 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
Manchikanti et al (150) A randomized trial with convenient control group. AHRQ Score 5/10	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
Manchikanti et al (151) Prospective evaluation in discogram-positive and discogram-negative chronic low back pain patients. AHRQ Score 5/8	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
Ciocon et al (156) A prospective evaluation in elderly patients suffering from degenerative lumbar canal stenosis. AHRQ Score 5/8	30 patients 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

laminectomy syndrome. The evidence is moderate in managing chronic low back pain for short-term and long-term improvement.

Complications

Our search strategy yielded a total of 287 results. The most common and worrisome complications 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 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 (21, 157-217). 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.

Houten and Errico (187) reported 3 cases of paraplegia after lumbosacral nerve root block in post laminectomy patients. They reported that in each case (performed at three different facilities, in the hands of two different physicians), the needle placement was verified with injection of contrast in conjunction with computerized tomography or biplanar fluoroscopy. In each patient, paraplegia was reported suddenly after injection of a steroid solution, and in each instance, post procedure magnetic resonance imaging 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 the 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 (187). This artery travels with the nerve root through the neural foramen, supplying the anterior spinal cord (187). Injury of the artery or injection of particulate steroid may result in infarction of the lower thoracic spinal cord.

Cousins (205) described a potential complication related to inadvertent intravascular administration of particulate depo-corticosteroids producing occlusion of small end arteries, which resulted in visual defects in one case, and hearing loss in another case, after a suboccipital nerve block. It is felt that methylprednisolone acetate tends to form aggregates of steroid material when mixed with local anesthetic and may pose more of a risk for this problem than other depo-steroids.

Brouwers et al (189) reported a cervical anterior spinal artery syndrome after diagnostic blockade of right C6 nerve root with fatal cervical spinal cord infarction. Nash (190) reported that he was aware of 3 cases with persistent neurological deficit following root sleeve injections of cervical and lumbar regions. Other transforaminal disasters have been described (183, 184, 197).

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, and betamethasone acetate and phosphate mixture have all been shown to be safe at epidural therapeutic doses in both clinical and experimental studies (207-216).

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 cervical and lumbar, and for axial, radicular and post laminectomy pain.

This systematic review arrived at the following conclusions. 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 is moderate for short-term improvement and long-term improvement. However, the evidence is inconclusive 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 is strong with short-term and long-term improvement. The evidence for cervical transforaminal epidural steroid injections in managing cervical nerve root pain, is strong with short-term and long-term improvement. The evidence is moderate in managing lumbar radicular pain in post lumbar laminectomy syndrome, with short-term and long-term improvement. The evidence of lumbar transforaminal epidural steroid injections in managing lumbar spinal stenosis is limited. The evidence is 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 is strong for short-term relief and moderate for long-term relief, in managing chronic pain of lumbar radiculopathy and post lumbar laminectomy syndrome. The evidence is moderate in managing chronic low back pain for short-term and long-term improvement. The evidence is limited for lumbar spinal stenosis.

The first systematic review of effectiveness of epidural steroid injections was performed by Kepes and Duncalf in 1985 (40). They concluded that the rationale for epidural and systemic steroids was not proven. However, in 1986 Benzon (42), 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 (40) and Benzon (42) may have been due to the fact that Kepes and Duncalf (40) included studies on systemic steroids whereas Benzon (41) 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 (21). In this report, Bogduk et al (21) 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 (42) 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 (43) 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 (44) 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 (45) 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 (46), 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 (46) 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 (47) 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.

The present systematic review is different from all the previous systematic reviews. The present systematic review has several additional features: epidural steroid injections involving cervical and lumbar regions were evaluated; radicular pain, axial pain, post lumbar laminectomy pain, and pain due to spinal stenosis; randomized and observational studies were taken into consideration; the review was performed by physicians who performed these procedures routinely, although none of the reviewed studies were conducted by these physicians. Consequently, we have reached different conclusions than the previous studies.

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 three techniques discussed in order to improve safety and minimize complications.

Conclusion

This systematic review, which included not only randomized trials, but also all available non-randomized trials, showed variable effectiveness of epidural injections.

The evidence ranged from indeterminate to strong based on the condition involved, the region involved, and pathology. It is crucial to understand the available evidence so that evidence based medical approach can be used when selecting these interventional procedures for our patients.

Appendix A. ***AHRQ's key domains (appearing in intalics) or systems to rate quality of randomized controlled studies*** (48).

Study Question
Study Population
Randomization
Blinding
Interventions
Outcomes
Statistical Analysis
Results
Discussion
Funding or Sponsorship

Appendix B. ***AHRQ's key elements for systems to rate quality of randomized controlled trials*** (48).

Elements appearing in italics are those with an empirical basis. Elements appearing in bold are those considered essential to give a system a Yes rating for the domain. For purposes of this systematic review, the bold elements were considered, and to be included studies needed to have at least 5 of the 10 essential elements.

- **Specific inclusion and exclusion criteria**
- *Adequate approach to sequence generation*
- ***Adequate concealment method used***
- *Similarity of groups at baseline*
- ***Double-blinding (e.g., of investigators, caregivers, subjects, assessors, and other key study personnel as appropriate) to treatment allocation***
- **Intervention(s) clearly detailed for all study groups (e.g., dose, route, timing for drugs, and details sufficient for assessment and reproducibility for other types of interventions)**
- **Primary and secondary outcome measures specified**
- ***Appropriate analytic techniques that address study withdrawals, loss to follow-up, missing data, and intention to treat***
- **Measure of effect for outcomes and appropriate measure of precision**
- **Conclusions supported by results with possible biases and limitations taken into consideration**
- ***Type and sources of support for study***

Appendix C. ***AHRQ's key domains or systems to rate quality of observational studies*** (48).

†Domain for which a Yes rating required that a majority of elements be considered.

Study Question
Study Population
Comparability of Subjects†
Exposure or Intervention

Outcome Measurement
Statistical Analysis
Results
Discussion
Funding or Sponsorship

Appendix D. ***AHRQ's key elements for systems to rate quality of observational studies*** (48).

*Elements appearing in italics are those with an empirical basis. Elements appearing in bold are those considered essential to give a system a Yes rating for the domain. For purposes of this systematic review, the bold elements were considered, and to be included studies needed to have at least 5 of the 8 essential elements.

- **Clearly focused and appropriate question**
- **Description of study populations**
- *Use of concurrent controls*
- **Clear definition of exposure**
- **Primary/secondary outcomes clearly defined**
- **Assessment of confounding factors**
- **Measure of effect for outcomes and appropriate measure of precision**
- **Conclusions supported by results with possible biases and limitations taken into consideration**
- ***Type and sources of support for study***

Appendix E. ***Methodologic quality criteria list (key items of internal validity) of Cochrane Musculoskeletal Review Group*** (49).

Patient selection

1. *Treatment allocation*
   Was the method of randomization described and adequate?
   Was the treatment allocation concealed?
2. *Were the groups similar at baseline regarding the most important prognostic indicators?*

Intervention

3. *Was the care provider blinded?*
4. *Was controlled for co-interventions which could explain the results?*
5. *Was the compliance rate (in each group) unlikely to cause bias?*
6. *.. Was the patient blinded?*

Outcome measurement

7. *Was the outcome assessor blinded?*
8. *Was at least one of the primary outcome measures applied?*
9. *Was the withdrawal/drop-out rate unlikely to cause bias?*

Statistics

10. *Did the analysis include an intention-to-treat analysis?*

Appendix F. ***Inclusion/exclusion criteria*** (50).

1. Are the patients described in sufficient detail to allow you to decide whether they are comparable to those that are seen in clinical practices of interventional pain management?
   A) Setting – office, hospital, outpatient, inpatient
   B) Physician – interventional pain physician, general physician, anesthesiologist, physiatrist, neurologist, rheumatologist, orthopedic surgeon, neurosurgeon, etc.
   C) Patient characteristics - duration of pain
   D) Non-interventional techniques or surgical intervention in the past
   E) Exclusion criteria
   F) Inclusion criteria
2. Is the intervention described well enough to enable you to provide the same for patients in interventional pain management settings?
   A) Nature of intervention
   B) Frequency of intervention
   C) Duration of intervention
3. Were clinically relevant outcomes measured?
   A) Proportion of pain relief
   B) Disorder/specific disability
   C) Functional improvement
   D) Allocation of eligible and non-eligible patients to return to work
   E) Ability to work
   F)Psychological assessment or improvement

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