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Systematic Review

Lumbar Interlaminar Epidural Injections in Managing Chronic Low Back and Lower Extremity Pain: A Systematic Review

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Background: Low back pain with or without lower extremity pain is the most common problem among chronic pain disorders with significant economic, societal, and health impact. Epidural injections are one of the most commonly performed interventions in the United States in managing chronic low back pain. However the evidence is highly variable among different techniques utilized – namely interlaminar, caudal, transforaminal – and for various conditions, namely – intervertebral disc herniation, spinal stenosis, and discogenic pain without disc herniation or radiculitis.

Study Design: A systematic review of lumbar interlaminar epidural injections with or without steroids.

Objective: To evaluate the effect of lumbar interlaminar epidural injections with or without steroids in managing various types of chronic low back and lower extremity pain emanating as a result of disc herniation or radiculitis, spinal stenosis, and chronic discogenic pain.

Methods: Review of the literature and methodologic quality assessment were performed according to the Cochrane Musculoskeletal Review Group Criteria as utilized for interventional techniques for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) criteria for observational studies.

The level of evidence was classified as Level I, II, or III based on the quality of evidence developed by the U.S. Preventive Services Task Force (USPSTF) for therapeutic interventions.

Data sources included relevant literature of the English language identified through searches of PubMed and EMBASE from 1966 to November 2008, and manual searches of bibliographies of known primary and review articles. Results of analysis were performed for multiple conditions separately.

Outcome Measures: The primary outcome measure was pain relief (short-term relief = up to 6 months and long-term > 6 months). Secondary outcome measures were improvement in functional status, psychological status, return to work, and reduction in opioid intake.

Results: The available literature included only blind epidural injections without fluoroscopy. The indicated evidence is positive (Level II-2) for short-term relief of pain of disc herniation or radiculitis utilizing blind interlaminar epidural steroid injections with lacking of evidence with Level III for long-term relief for disc herniation and radiculitis. The evidence is lacking with Level III for short and long-term relief for spinal stenosis and discogenic pain without radiculitis or disc herniation utilizing blind epidural injections.

Limitations: The limitations of this study include paucity of literature, lack of quality evidence, lack of fluoroscopic procedures, and lack of applicable evidence in contemporary interventional pain management practices.

Conclusion: The evidence based on this systematic review is limited for blind interlaminar epidurals in managing all types of pain except for short-term relief of pain secondary to disc herniation and radiculitis. This evidence does not represent contemporary interventional pain management practices and also the evidence may not be extrapolated to fluoroscopically directed lumbar interlaminar epidural injections.

Key words: Chronic low back pain, lower extremity pain, disc herniation, radiculitis, spinal stenosis, discogenic pain, lumbar interlaminar epidural injections, caudal epidural injections, transforaminal epidural injections, epidural steroids, local anesthetic

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Low back pain with or without lower extremity pain is the most common problem among chronic pain disorders with significant economic, societal, and health impact (1-12). Chronic low back pain is a multifactorial disorder with many possible etiologies. Kuslich et al (13) identified intervertebral discs, facet joints, ligaments, fascia, muscles, and nerve root dura as tissues capable of transmitting pain in the low back. A widespread interest was created in the disc as a source of pain in American literature by Mixter and Barr (14) in 1934 with their hallmark description of the herniated nucleus pulposus. In addition, Mixter and Ayers (15), just one year after the original description in 1934, demonstrated that radicular pain can occur without disc herniation. Subsequently, numerous investigators (16-24) have described pain syndromes emanating from lumbar intervertebral disc without mechanically compressing neural structures. Consequently, the pathophysiology of spinal radicular pain is a subject of ongoing research and controversy and discogenic pain has assumed a major role as a cause of non-specific low back pain, beyond the more specific cause of disc herniation. Thus, in addition to the mechanical component, inflammation of the compressed nerve root is an important factor in the pathophysiology of radicular and discogenic pain (22,24-31). Other proposed etiologies include neural compression with dysfunction and vascular compromise (32-36). Further, neurotoxicity has been attributed to many agents including phospholipase A2 (PLA_2) and tumor necrosis factor (TNFα) which may play an essential role in intervertebral disc-induced nerve root damage (18,26-30,37-40).

Intervertebral disc herniation, spinal stenosis, intervertebral disc degeneration without disc herniation, degenerative spondylolisthesis with stenosis, and post lumbar surgery syndrome are the most common diagnoses of low back and leg symptoms (14-21,41-51).

Epidural injections are the most commonly performed interventions in the United States in managing chronic low back pain (52-58). Among several approaches available to access the lumbar epidural space, the lumbar interlaminar approach is the most commonly used, the other 2 being the lumbar transforaminal approach and caudal approach (1,58,59). The interlaminar approach has been touted as its entry can be directed more closely to the assumed site of pathology, requiring less volume than the caudal route and it is less risky compared to the transforaminal approach which is considered to be a more target-specific approach requiring the smallest volume to reach the primary site of pathology.

However, epidural procedures continue to be controversial regarding their effectiveness, indications, and medical necessity (1,58-73). The evidence is highly variable based on the reviewer with ratings ranging from indeterminate to moderate in various publications. The majority of the literature on lumbar interlaminar epidurals appears to be negative. The first systematic review of the effectiveness of epidural steroid injections was performed by Kepes and Duncalf in 1985 (61) which concluded that the rationale for epidural and systemic steroids had not been proven. However, in a follow-up systematic review in 1986, Benzon (73), 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 differences in the conclusions of Kepes and Duncalf (61) and Benzon (73) may have been due to the fact that Kepes and Duncalf (61) included studies on systematic steroids, whereas Benzon (73) limited his analysis to studies on epidural steroid injections only.

Bogduk et al (59) extensively reviewed caudal, interlaminar, and transforaminal epidural injections, including all of the literature available at that time. They concluded that the results of lumbar interlaminar epidural steroids strongly refute the utility of epidural steroids in acute sciatica. Bogduk (60) updated their recommendations in 1999, recommending against epidural steroids by the lumbar route because effective treatment required too high a number for successful treatment. In 1995, Koes et al (62) reviewed 12 trials of lumbar and caudal epidural steroid injections (combined together) and reported positive results from only 6 studies, concluding that there was no evidence for epidural steroids in managing lumbar radicular pain. Their updated review (63) with 15 trials arrived at similar conclusions that there was no evidence that epidural steroid injections are effective in patients with chronic back pain without sciatica. Overall, the evidence for lumbar interlaminar epidural steroid injections is limited in managing pain secondary to disc herniation. However, available evidence is even inferior in managing axial low back pain and lumbar spinal stenosis (58,65,66).

The underlying mechanism of action of epidurally administered local anesthetic and steroid injections is not well understood. However, multiple hypotheses have been presented indicating pain relief by vari-

ous mechanisms both by steroids and local anesthetics (74-87). In fact, the effect of local anesthetic with or without steroids has been reported to be the same in epidural injections in clinical studies (88-91), facet joint nerve blocks (78-80), as well as in an experimental evaluation of nerve root infiltration (87).

Due to the ongoing controversy and lack of significant evidence, this systematic review is undertaken to evaluate the effects of lumbar interlaminar epidural injections in managing chronic low back and lower extremity pain secondary to lumbar disc herniation and radiculitis, spinal stenosis, and chronic low back pain of discogenic origin without radiculitis or disc herniation.

Methods

Literature Search

A comprehensive literature search was conducted which included the search of databases including PubMed and EMBASE from 1966 through November 2008, Cochrane database, Clinical Trial Registry, systematic reviews, narrative reviews, and cross-references to the reviews published in the English language.

The search strategy emphasized chronic low back pain of discogenic origin with a focus on lumbar epidural injections. Search terminology included lumbar intervertebral disc, disc-related pain, spinal stenosis, and lumbar epidural injections.

Selection Criteria

The review focused on randomized trials and observational studies, and reports of complications. The population of interest was patients suffering with chronic low back pain for at least 3 months. Only lumbar interlaminar epidural injections with or without steroids were evaluated. All the studies providing appropriate management with outcome evaluations of 6 months or longer and statistical evaluations were reviewed. Reports without appropriate diagnosis, non-systematic reviews, book chapters, and case reports were excluded.

Outcome Parameters

The outcome measures were of documented pain relief at various points in time, functional assessment, and other outcomes including psychological improvement, return to work, and change in opioid intake.

Methodologic Quality Assessment

The quality of each individual article used in this analysis was assessed by modified Cochrane review criteria with weighted scores (Table 1) (62) for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) quality criteria for assessment of observational studies (Table 2) (92) with consensus-based weighted scoring developed by the guidelines committee of the American Society of Interventional Pain Physicians (ASIPP) utilized in multiple evaluations (70,93-97).

Only the studies scoring at least 50 of 100 on weighted scoring criteria were utilized for analysis.

Each study was evaluated by 2 physicians for stated criteria and any disagreements were resolved by a third physician.

If there was a conflict of interest with the reviewed manuscripts with authorship or any other type of conflict, the involved authors did not review the manuscripts for quality assessment or evidence synthesis.

Clinical Relevance

Clinical relevance of the included studies was evaluated according to 5 questions recommended by the Cochrane Back Review Group (66,98-100).

Table 3 shows the clinical relevance questions. Each question was scored positive (+) if the clinical relevance item was met, negative (–) if the item was not met, and unclear (?) if data were not available to answer the question.

In the recent Cochrane review of "Injection Therapy for Subacute and Chronic Low Back Pain" (66) the authors considered a 20% improvement in pain scores (98) and a 10% improvement in functioning outcomes (99) to be clinically important. The current study utilized stricter criteria than general systematic reviews and previous systematic reviews. Any relief of 6 months or less was considered as short-term, whereas Cochrane reviews (66) and others have considered 6 weeks as short-term and longer than 6 weeks as long-term. We also utilized methodologic quality assessment criteria (66) for minimum inclusion, thus this systematic review is expected to provide robust results with stricter criteria. However, in contrast to many other systematic reviews, we have not excluded observational studies and included only quality observational studies with scores of 50 or more on a scale of 0–100 based on AHRQ criteria. This improves the generalizability of the systematic review and the intervention. However, in interventional pain management settings, significant improvement has been defined as 50% or more relief, whereas significant improve-

Table 1. *Modified and weighted Cochrane methodologic quality assessment criteria.*

CRITERION		Weighted Score (points)
1. Study population		**35**
A	Homogeneity	2
B	Comparability of relevant baseline characteristics	5
C	Randomization procedure adequate	4
D	Drop-outs described for each study group separately	3
E	< 20% loss for follow-up	2
	< 10% loss for follow-up	2
F	> 50 subject in the smallest group	8
	> 100 subjects in the smallest group	9
2. Interventions		**25**
G	Interventions included in protocol and described	10
H	Pragmatic study	5
I	Co-interventions avoided or similar	5
J	Placebo-controlled	5
3. Effect		**30**
K	Patients blinded	5
L	Outcome measures relevant	10
M	Blinded outcome assessments	10
N	Follow-up period adequate	5
4. Data-presentation and analysis		**10**
O	Intention-to-treat analysis	5
P	Frequencies of most important outcomes presented for each treatment group	5
	TOTAL SCORE	100

Adapted from Koes BW et al. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. *Pain* 1995; 63:279-288 (62).

ment in disability has been defined as a 40% or more decrease in disability scores in multiple publications (78-80,88-91,101-104).

Analysis of Evidence

Quality analysis was conducted using 5 levels of evidence, ranging from Level I to III with 3 subcategories in Level II, as illustrated in Table 4 (105).

Grading recommendations were based on Guyatt et al's criteria as illustrated in Table 5 (106).

Outcome of the Studies

A study is judged to be positive if the epidural injection therapy was effective, either with a placebo control or active control in randomized trials. This indicates that the difference in the effect for the primary outcome measure was statistically significant at the conventional 5% level. In a negative study, no difference was reported between the study treatments or no improvement from baseline. Further, the outcomes were judged at the reference point with positive or negative results reported at 3 months, 6 months, and one year.

For observational studies, a study was judged to be positive if the epidural injection therapy was effective, with outcomes reported at the reference point with positive or negative results at 3 months, 6 months, and one year. Relief of 6 months or less was considered as short-term and relief of longer than 6 months was considered as long-term.

The data will be analyzed separately for disc herniation and/or radiculopathy, discogenic pain with

Table 2. *Modified AHRQ quality assessment criteria for observational studies.*

CRITERION	Weighted Score (points)
1. Study Question	2
• Clearly focused and appropriate question	
2. Study Population	8
• Description of study population	5
• Sample size justification	3
3. Comparability of Subjects	22
• Specific inclusion/exclusion criteria for all groups	5
• Criteria applied equally to all groups	3
• Comparability of groups at baseline with regard to disease status and prognostic factors	3
• Study groups comparable to non-participants with regard to confounding factors	3
• Use of concurrent controls	5
• Comparability of follow-up among groups at each assessment	3
4. Exposure or Intervention	11
• Clear definition of exposure	5
• Measurement method standard, valid and reliable	3
• Exposure measured equally in all study groups	3
5. Outcome measures	20
• Primary/secondary outcomes clearly defined	5
• Outcomes assessed blind to exposure or intervention	5
• Method of outcome assessment standard, valid and reliable	5
• Length of follow-up adequate for question	5
6. Statistical Analysis	19
• Statistical tests appropriate	5
• Multiple comparisons taken into consideration	3
• Modeling and multivariate techniques appropriate	2
• Power calculation provided	2
• Assessment of confounding	5
• Dose-response assessment if appropriate	2
7. Results	8
• Measure of effect for outcomes and appropriate measure of precision	5
• Adequacy of follow-up for each study group	3
8. Discussion	5
• Conclusions supported by results with possible biases and limitations taken into consideration	
9. Funding or Sponsorship	5
• Type and sources of support for study	
TOTAL SCORE	**100**

Adapted and modified from West S et al. Systems to Rate the Strength of Scientific Evidence, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016 (92).

Table 3. *Clinical relevance questions.*

A)	Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?
B)	Are the interventions and treatment settings described well enough so that you can provide the same for your patients?
C)	Were all clinically relevant outcomes measured and reported?
D)	Is the size of the effect clinically important?
E)	Are the likely treatment benefits worth the potential harms?

Source: Staal JB et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (66).

Table 4. *Quality of evidence developed by USPSTF.*

I:	**Evidence obtained from at least one properly randomized controlled trial**
II-1:	**Evidence obtained from well-designed controlled trials without randomization**
II-2:	**Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group**
II-3:	**Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence**
III:	**Opinions of respected authorities, based on clinical experience descriptive studies and case reports or reports of expert committees**

Adapted from the U.S. Preventive Services Task Force (USPSTF) (105).

Table 5. *Grading recommendations*.

Grade of Recommendation/ Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Adapted from Guyatt G et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181 (106).

predominantly low back pain, and spinal stenosis.

Studies performed under fluoroscopy were given priority.

Observational studies were only included in the evidence synthesis if there were less than 4 randomized trials meeting inclusion criteria for each category as described above. If a study included more than one type of patient and the analysis in the study was considered separately for both conditions, that study was included for all the conditions.

Results

A literature search was carried out for lumbar interlaminar epidural injections as shown in Fig. 1.

Our search strategy yielded multiple studies evaluating the effectiveness of interlaminar epidural injections with or without steroids. These included 20 randomized or double-blind trials (107-126) and 30 observational studies (127-156).

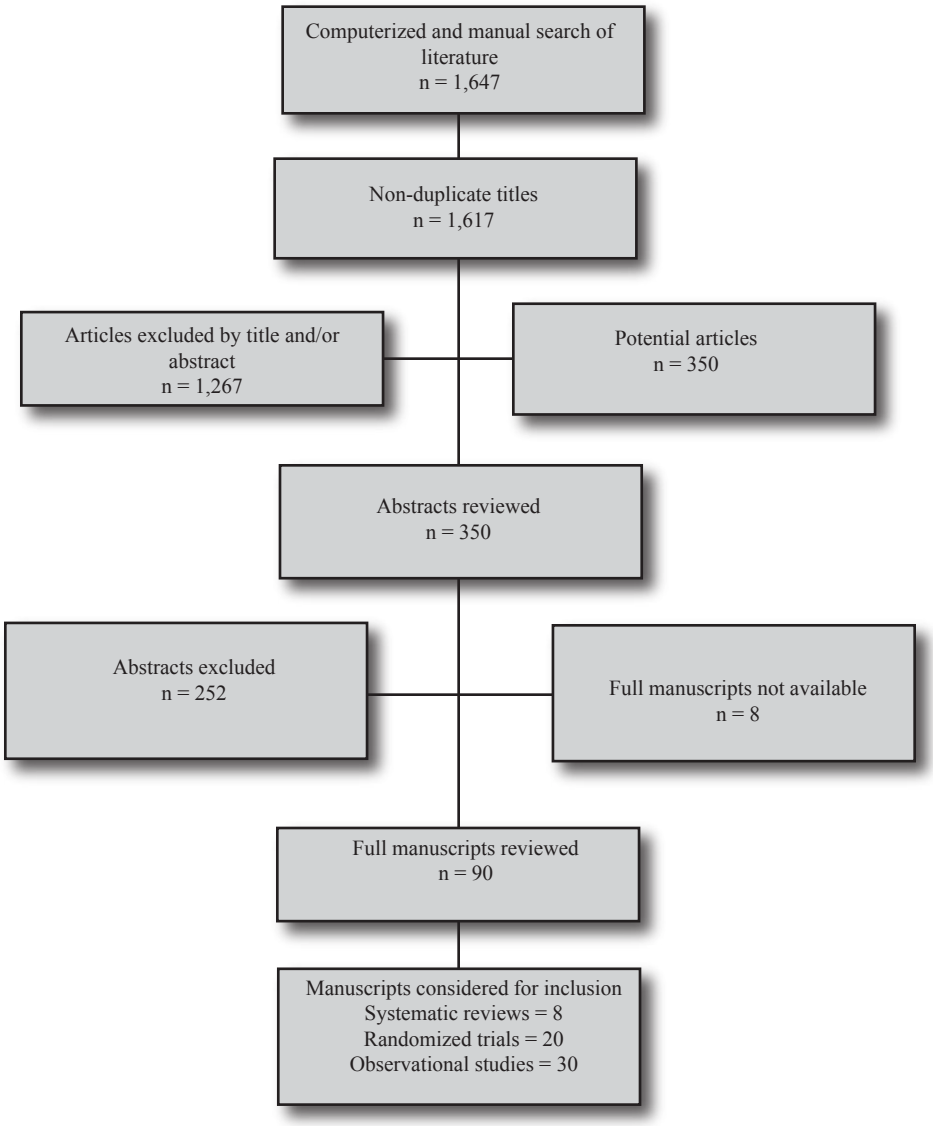

Fig. 1. *The flow diagram illustrating randomized trials, observational studies, and systematic reviews evaluating caudal epidural injections.*

Randomized Trials

Methodologic Quality Assessment

Of the 20 randomized trials, 11 studies met inclusion criteria (107-111,115,116,122,123,125,126). Of these, 6 studies met the inclusion criteria to be included for methodological assessment (108-110,115,125,126). Reasons for exclusion were as follows:

- Serrao et al (112) was excluded as they studied the effects of subarachnoid and epidural midazolam.
- Two studies (117,118) were excluded since they focused on diabetic polyneuropathy and intractable post-herpetic neuralgia.
- Buchner et al (120) was excluded as they evaluated only inpatients.
- Multiple evaluations (107,111,113,114,116,121-124) were excluded for lack of evaluation of long-term outcomes.

Methodological quality criteria are illustrated in Table 6 showing all the randomized clinical trials evaluating the effectiveness of lumbar interlaminar epidural injections. The quality assessment criteria

Table 6. *Methodological assessment of randomized trials evaluating the effectiveness of lumbar interlaminar epidural injections.*

CRITERION		WEIGHTED SCORE (points)	Arden et al (126)	Carette et al (108)	Cuckler et al (110)	Wilson-MacDonald et al (125)	Snoek et al (109)	Ridley et al (115)
Study population								
A	Homogeneity	2	2	2	2	2	2	2
B	Comparability of relevant baseline characteristics	5	5	5	4	5	3	4
C	Randomization procedure adequate	4	4	4	4	4	4	2
D	Drop-outs described for each study group separately	3	3	3	3	3	3	—
E	< 20% loss for follow-up	2	—	—	2	2	2	2
	< 10% loss for follow-up	2	—	—	2	2	2	—
F	> 50 subject in the smallest group	8	8	8	—	—	—	—
	> 100 subjects in the smallest group	9	9	—	—	—	—	—
Interventions								
G	Interventions included in protocol and described	10	10	10	10	10	10	10
H	Pragmatic study	5	—	—	5	—	—	—
I	Co-interventions avoided or similar	5	—	—	—	—	5	—
J	Placebo-controlled	5	5	5	—	—	5	5
Effect								
K	Patients blinded	5	5	5	3	5	3	3
L	Outcome measures relevant	10	10	10	2	10	8	4
M	Blinded outcome assessments	10	10	10	10	10	10	10
N	Follow-up period adequate	5	5	5	5	5	5	5
Data-presentation and analysis								
O	Intention-to-treat analysis	5	5	5	5	5	5	—
P	Frequencies of most important outcomes presented for each treatment group	5	5	5	3	5	5	—
	TOTAL SCORE	100	86	77	60	68	72	47

Methodological criteria and scoring adapted from Koes BW et al. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. *Pain* 1995; 63:279-288 (62).

ranged from 47 to 86 with 5 of 6 trials meeting inclusion criteria.

Clinical Relevance Assessment

Table 7 illustrates the clinical relevance of randomized trials. The scores were 3 of 5 for all the trials.

Inclusion Criteria

Of the 5 studies meeting inclusion criteria for evidence synthesis, 4 of them (108,109,125,126) included patients with disc herniation and sciatica, whereas one study (110) included patients with acute herniated nucleus pulposus or spinal stenosis of longer than 6 months.

There were no randomized trials evaluating the patients either with spinal stenosis alone or with chronic low back pain of discogenic origin without radiculitis.

Observational Studies

Of the 30 observational studies (127-156), 2 studies were excluded as they were not related to the lumbar interlaminar procedure (139,146). One study was excluded due to factor analysis rather than outcome assessment (138). Five studies were excluded due to short-term follow up (129,141,143,149,155). One study (131) was excluded due to short-term relief and the procedure was being performed in an inpatient setting. Seven studies were excluded due to non-availability of full manuscripts or data for methodology quality assessment (127,130,132,133,144,153,154).

Methodologic Quality Assessment

Methodologic quality assessment was performed on the studies evaluating either spinal stenosis or discogenic pain. No observational studies were included for disc herniation or radiculitis as 6 randomized trials (108-110,115,125,136) met inclusion criteria.

Among the observational studies meeting the inclusion criteria for evidence synthesis, one evaluation studied chronic discogenic low back pain without radiculitis (148) and one study evaluated spinal stenosis (150). Of all the studies meeting inclusion criteria, only one study by Butterman (148) was performed under fluoroscopy. There was only one study meeting inclusion criteria evaluating the role of epidural steroid injections in spinal stenosis.

Methodologic quality assessment criteria are illustrated in Table 8. Butterman (148) scored 75, whereas Campbell et al (150) scored 53, thus both of them met inclusion criteria.

Disc Herniation and Radiculitis

Of the studies meeting inclusion criteria (108-110,126,127), Cuckler et al (110) studied patients with either acute herniated nucleus pulposus or spinal stenosis of greater than 6 months. Of the 73 patients with back pain included in the study, 34 were secondary to acute herniated nucleus pulposus, whereas 37 patients were secondary to spinal stenosis reducing the sample size (110). Wilson-MacDonald et al (125) included 32 patients with spinal stenosis, with 43 patients with disc herniation. All other studies evaluated the role of epidural injections in sciatica or radiculitis.

Table 7. *Assessment of clinical relevance of randomized clinical trials evaluating the effectiveness of lumbar interlaminar epidural injections.*

	Arden et al (126)	Carette et al (108)	Cuckler et al (110)	Wilson-MacDonald (125)	Snoek et al (109)
A) «Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?	+	+	+	+	+
B) «Are the interventions and treatment settings described well enough so that you can provide the same for your patients?	-	-	-	-	-
C) «Were all clinically relevant outcomes measured and reported?	+	+	+	+	+
D) «Is the size of the effect clinically important?	+	+	+	+	+
E) «Are the likely treatment benefits worth the potential harms?	-	-	-	-	-
TOTAL CRITERIA MET	3/5	3/5	3/5	3/5	3/5

+ = positive; - = negative; ? = unclear
Scoring adapted from Staal JB et al. Injection therapy for subacute and chronic low-back pain. Cochrane Database Syst Rev 2008; 3:CD001824 (66).

Table 8. *Methodological assessment of observational studies evaluating the effectiveness of lumbar interlaminar epidural injections.*

CRITERION	Weighted Score (points)	Butterman (148)*	Campbell et al (150)
1. Study Question	2	2	2
• Clearly focused and appropriate question		2	2
2. Study Population	8	5	5
• Description of study population	5	5	5
• Sample size justification	3	--	--
3. Comparability of Subjects for All Observational Studies	22	14	5
• Specific inclusion/exclusion criteria for all groups	5	5	5
• Criteria applied equally to all groups	3	3	--
• Comparability of groups at baseline with regard to disease status and prognostic factors	3	3	--
• Study groups comparable to non-participants with regard to confounding factors	3	--	--
• Use of concurrent controls	5	--	--
• Comparability of follow-up among groups at each assessment	3	3	--
4. Exposure or Intervention	11	11	6
• Clear definition of exposure	5	5	5
• Measurement method standard, valid and reliable	3	3	1
• Exposure measured equally in all study groups	3	3	--
5. Outcome measures	20	15	10
• Primary/secondary outcomes clearly defined	5	5	5
• Outcomes assessed blind to exposure or intervention	5	--	--
• Method of outcome assessment standard, valid and reliable	5	5	--
6. Statistical Analysis	19	10	10
• Statistical tests appropriate	5	5	5
• Multiple comparisons taken into consideration	3	3	3
• Modeling and multivariate techniques appropriate	2	2	2
• Power calculation provided	2	--	--
• Assessment of confounding	5	--	--
• Dose-response assessment if appropriate	2	--	--
7. Results	8	8	5
• Measure of effect for outcomes and appropriate measure of precision	5	5	2
• Adequacy of follow-up for each study group	3	3	3
8. Discussion	5	5	5
• Conclusions supported by results with possible biases and limitations taken into consideration		5	5
9. Funding or Sponsorship	5	5	5
• Type and sources of support for study		5	5
TOTAL SCORE	100	75	53

*Performed utilizing fluoroscopy

Adapted and modified from West S et al. Systems to Rate the Strength of Scientific Evidence, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016 (92).

Study Characteristics

Table 9 shows the characteristics of randomized trials of lumbar interlaminar epidural injections evaluating disc herniation and radiculitis. Surprisingly, none of the studies were performed under fluoroscopy.

Cuckler et al (110) performed a prospective, randomized, double-blind study of the use of epidural steroids in the treatment of lumbar radicular pain. They included 73 patients with a clinical diagnosis of either acute herniated nucleus pulposus or spinal stenosis

Table 9. *Characteristics of published randomized trials of blind lumbar interlaminar epidural injections in managing disc herniation and radiculitis.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 mos. Long-term relief > 6 mos.
Wilson-Mac-Donald et al 2005 (125) Randomized, controlled trial	93 pts. with MRI evidence of a disc prolapse, spinal stenosis, or a combination. Pts. had lumbosacral nerve root pain which had not resolved within 6 wks minimum. 32 pts. with 18 into the epidural group and 14 in the control group had spinal stenosis only, whereas 3 pts. in the epidural group and 15 pts. in control group had a combined disc herniation and spinal stenosis.	Experimental: epidural injection of bupivacaine 0.5% (40 mg) with methyl-prednisolone 80 mg. Control: intramuscular injection of 0.5% (40 mg) bupivacaine with 80 mg methylprednisolone.	Timing: 6 wks, 24 mos. Outcome measures: Oswestry Disability index, pain relief.	In the first 5 wks after epidural injection a useful improvement in nerve root symptoms was seen.	Positive short-term and negative long-term relief
Arden et al 2005 (126) Double-blind, randomized placebo controlled: TRIM	228 pts. with unilateral sciatica.	Experimental: triamcinolone 80 mg and 10 mL of 0.25% bupivacaine. Control: interspinous injection with 2 mL of normal saline.	Timing: 3, 6, 12, 26, and 52 weeks. Outcome measures: Oswestry disability index, Likert scale, SF-36, VAS.	Lumbar epidural steroid injection produced a statistically significant improvement in function over placebo in 3 wks. By 6 wks, benefit lost.	Negative short- and long-term relief
Carette et al 1997 (108) Randomized, double-blind trial	158 pts. with sciatica due to a herniated nucleus pulposus. Treatment group: 78 Placebo group: 80	Experimental: methylprednisolone acetate (80 mg and 8 mL of isotonic saline) Control: isotonic saline 1 mL Frequency: 3 epidural injections 3 wks. apart.	Timing: 6 wks., 3 mos., 12 mos. Outcome measures: need for surgery, Oswestry Disability scores.	Significant improvement was seen in leg pain in the methylprednisolone group after 6 weeks, with no difference after 3 and 12 mos.	Positive short-term and negative long-term relief
Cuckler et al 1985 (110) Randomized, double-blind trial	73 pts. with back pain due to either acute herniated nucleus pulposus or spinal stenosis of > 6 mos. Experimental: 42 Control: 3.1	Experimental: 80 mg (2 mL) of methylprednisolone + 5 mL of procaine 1%. Control group: 2 mL saline + 5 mL of procaine 1%.	Timing: 24 hrs and an average of 20 mos. Outcome measures: subjective improvement, need for surgery.	There was no significant short-term or long-term improvements between both groups.	Negative short-term and long-term relief
Snoek et al 1977 (109) Randomized trial	51 pts. with lumbar root compression documented by neurological deficit and a concordant abnormality noted on myelography. Experimental: 27 Control: 24	Experimental: 80 mg of methylprednisolone (2 mL). Control: 2 mL of normal saline Frequency: single injection.	Timing: 3 days and an average of 14 mos. Outcome measures: Pain, sciatic nerve stretch tolerance.	No statistically significant differences were noted in either group.	Negative short-term and long-term relief

between November 1978 and 1980. All the procedures were performed without fluoroscopy. Ninety percent of the epidural injections were performed by a single anesthesiologist in a lateral decubitus position, between the third and fourth lumbar vertebra, lying on the side of the painful limb. Either 2 mL of sterile water containing 80 mg of methylprednisolone acetate combined with 5 mL of 1% procaine or 2 mL of saline combined with 5 mL of 1% procaine was injected. The authors stated that neither the treating physician, nor the patient was informed of the contents of the initial injection until July 1981; however, they have not described the concealment process. They also provided a second injection if there had been less than 50% improvement 24 hours after the first injection with methylprednisolone acetate and procaine in a non-blind fashion. Further, they defined a short-term successful result as subject to improvement of 75% or more as judged by the patient 24 hours after injection. Anything less than 75% was considered as short-term failure. Further, they described all patients who received a second injection as having a failed result. They also defined any patient who had laminectomy during the period of follow-up (which was over 20 months) as a long-term failed result. They did not provide any special exercise program or other physical therapy. The long-term results showed 25 (61%) of 41 patients who received an epidural steroid injection as the first injection reported some degree of improvement, while 20 (62.5%) of the 32 patients who received placebo injection reported some degree of improvement.

These authors utilized a flawed process by considering local anesthetic injection as a placebo. Consequently, this is not an efficacy trial, but it is an equivalency or non-inferiority trial (78-80,88-91). Further, the effectiveness of local anesthetics has been demonstrated and shown to be equal to steroids, both in clinical and experimental studies (78-80,87-91,157-162). Further, when multiple variables are considered, the procedure was performed with a blind technique between L3 and L4 in the lateral decubitus position with the affected side down with inability to reach the targeted area in almost half of the patients (147,163-171). Other flaws of this study include small sample size, poor methodology, and inadequate outcome assessments. Statistically detailed data were not provided to calculate the patients receiving greater than 50% relief at any point in the evaluation. Further, evaluation was performed only at 2 points. Thus, the results of this study may not provide any value in contemporary interventional pain management.

Carette et al's (108) study has been described as the best study evaluating the role of epidural steroids in managing sciatica due to herniated nucleus pulposus. However, this study also contains numerous deficiencies. Between October 1992 and January 1996, they enrolled 158 patients with 78 patients in the methylprednisolone group and 80 patients in the placebo group. The patients received injections of either 80 mg (2 mL) of methylprednisolone acetate mixed with 8 mL of isotonic saline) or 1 mL of isotonic saline in the epidural space according to the technique described by Barry and Kendall (172), without fluoroscopy, in a physiatric practice, dating back to 1962. The procedure was performed without fluoroscopy in the lateral decubitus position and isotonic saline was administered, in fact, into the epidural space. No information is available with regards to the effect of injection of an inert substance into the epidural space. Further, the disadvantages of the spread of the drug, level of the injection, lack of ventral placement of the drug, and lack of fluoroscopy fail to generalize the results to contemporary interventional pain management practice. The results showed that at 3 weeks, the Oswestry Disability Index (ODI) score had improved slightly better in the methylprednisolone group compared to the placebo group, along with significant differences noted with finger-to-floor distance (P = 0.006) and sensory deficits (P = 0.003), which were greater in the methylprednisolone group. However, after 6 weeks, the only significant difference was the improvement in leg pain, which was greater in the methylprednisolone group (P = 0.03). After 3 months, there were no significant differences between the groups. Further, at 12 months, the cumulative probability of back surgery was 25.8% in the methylprednisolone group and 24.8% in the placebo group. The authors concluded that even though epidural injections of methylprednisolone may afford short-term improvement in leg pain and sensory deficits in patients with sciatica due to a herniated nucleus pulposus, this treatment offers no significant functional benefit, nor does it reduce the need for surgery compared to saline epidural injection. However two-thirds of the patients in both groups avoided surgery.

Arden et al (126) in a study published in 2005 evaluated the effectiveness and predictors of response to lumbar epidural corticosteroid injections

in patients with sciatica, in a 12-month, multi-center, double-blind, randomized, placebo-controlled, parallel-group trial in 4 secondary pain-care clinics in the Wessex Region of the United Kingdom. They recruited 228 patients, aged 18 to 70 years, presenting to orthopaedic, rheumatology, and pain clinics at the participating hospitals with a clinical diagnosis of unilateral sciatica between 4 weeks and 18 months duration. Of these, one-third of the patients were acute and two-thirds were chronic. All the injections were performed by anesthetists experienced in the procedure. The details of the procedure are not provided, hence, it is assumed they were performed blindly without fluoroscopy and in the lateral position between L3-4 or L4-5. The active group received epidural steroids via the lumbar route of 80 mg of triamcinolone acetonide and 10 mL of 0.25% bupivacaine at weeks 0, 3, and 6. The placebo group received injections of 2 mL of normal saline into the intraspinous ligament. Sixty patients achieved a 75% improvement on the ODI before week 6 and therefore did not receive 3 injections. The patients were assessed at 3, 6, 12, 26, and 52 weeks, with the primary outcome measure being the ODI and the criterion of response being a reduction of 75% from baseline, with secondary outcome measures of visual analog scale (VAS) and the Short-Form-36 (SF-36) questionnaire, etc. Based on the available literature, a reduction of 75% from baseline on the ODI is an unusual and unrealistic outcome measure as the literature considers a clinically important difference as an improvement of 4 points to 15 points (102-104,173-175). Even then, they reported a statistically significant improvement in self-reported function compared with placebo at 3 weeks. At the same time they reported that lumbar epidural corticosteroid injections did not produce a significant improvement in VAS leg pain, but did increase the number of patients reporting any improvement in leg pain using the Likert scale (61% versus 40%, $P < 0.01$). However, they reported that by 6 weeks the benefit of epidural steroids was lost, and at all subsequent visits there were no differences between the groups on any measures of outcome. At 52 weeks, 32.5% of the active group and 29.6% of the placebo group had achieved a 75% improvement in ODI. Consequently, this result in both placebo and treatment group probably related to the natural course of the disease. Further, they also reported that after 12 months, 26 patients were pain free, with no difference between treatment groups, again illustrating the disadvantages of including patients with acute problems. Another outcome was that neurological symptoms and signs tended to improve throughout the trial, even though, at the end of the study, 44.8% of the patients still had decreased sensation and 24.6% decreased power. The authors describe that for the first time, a single large randomized controlled trial confirmed that epidural injections of corticosteroids offered short-term relief of symptoms in patients with sciatica at 3 weeks; however, they do not offer any medium- or long-term benefit in terms of symptoms, function, return to work, or the need for surgery. Further, the authors ignored many of the fundamental principles of contemporary interventional pain management, namely that no injections should be repeated unless the pain returns, the effect of steroids generally last approximately 4–6 weeks, and, by failing to use fluoroscopy, potentially providing non-targeted injections in approximately 50% to 80% of the patients.

Snoek et al (109) studied 51 patients with lumbar root compression documented by neurological deficit and a concordant abnormality noted on myelography. They compared the effects of 80 mg of methylprednisolone (2 mL) and 2 mL of normal saline injected into the epidural space by the lumbar route. They found no significant differences between the 2 groups with respective relief of pain and a variety of physical parameters.

Wilson-MacDonald et al (125) compared lumbar epidural steroid injections to interspinous ligament steroid injections, to assess whether the epidural location of the steroid was responsible for the subsequent effects. Ninety-three patients with back and leg pain and MRI evidence of a prolapsed disc who had been offered surgery were randomized to receive either a blind lumbar epidural (44 patients) or an injection into the interspinous ligament (48 patients). Each patient was injected with 8 mL 0.5% bupivacaine and 80 mg of methylprednisolone. There was no difference in the rate of subsequent surgery through the period of follow up.

Effectiveness

As shown in Table 10, of the 5 randomized trials (blind lumbar interlaminar epidurals) included in the evidence synthesis, 2 were positive for short-term and 5 of them providing long-term results were negative for long-term relief of more than 6 months.

Table 10. *Results of randomized trials of effectiveness of blind lumbar interlaminar epidural steroid injections in managing disc herniation and radiculitis.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief				Results	
				< 3 mos.	3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 mos.	Long-term relief > 6 mos.
Wilson-MacDonald et al 2005 (125)	RA	68	43	SIT	NSD	NSD	NSD	P	N
Arden et al 2005 (126)	RA,DB,PC	86	228	75%	NSD	NSD	NSD	N	N
Carette et al 1997 (108)	RA,DB,PC	77	C = 80 T = 78	SIT	NSD	NSD	NSD	P	N
Cuckler et al 1985 (110)	RA,DB	60	C = 31 T = 42	NSD	NSD	NSD	NSD	N	N
Snoek et al 1977 (109)	RA	72	C = 24 T = 27	NSD	NSD	NSD	NSD	N	N

RA = randomized; DB = double blind; PC = placebo controlled; C = control; T = treatment; SIT = significant improvement in treatment group; NSD = no significant difference; P = positive; N = negative; NA = not available

Spinal Stenosis

Two blind lumbar interlaminar randomized trials (110,125) and one blind lumbar interlaminar observational study (150) evaluating spinal stenosis were identified.

Study Characteristics

Cuckler et al (110) included 37 patients from a sample of 73 patients with spinal stenosis of longer than 6 months. They injected in a randomized, double blind fashion either 7 mL of methylprednisolone acetate and procaine or 7 mL of physiological saline solution and procaine. No statistically significant difference was observed between the control and experimental patients. Long-term follow-up, averaging 20 months, failed to demonstrate the efficacy of a second injection of epidural steroids administered to the patients whose pain did not respond within 24 hours to an injection of either 80 mg of methylprednisolone acetate combined with 5 mL of 1% procaine or 2 mL of sterile saline combined with 5 mL of 1% procaine. The multiple disadvantages of this study and various flaws are described in the disc herniation section.

Wilson-MacDonald et al (125) evaluated 18 patients in the epidural group and 14 patients in the control group with spinal stenosis only. Further, there were also 18 (control = 15, epidural = 3) patients with disc herniation and stenosis. Patients were treated either with an epidural steroid injection or an intramuscular injection of local anesthetic and steroids. Even though the results were negative, there was no significant difference in any of the groups on a long-term basis. However, there was a significant reduction in pain early on in those having an epidural steroid injection.

Campbell et al (150) in 2007 published results of the correlation of spinal canal dimensions to efficacy of epidural steroid injections in spinal stenosis. They included 84 patients in the study, 50 required surgical decompression after epidural steroid injection and 34 patients improved after epidural steroid injection. All the patients received lumbar interlaminar epidural injections. They concluded that spinal canal dimension is not predictive of success or failure of epidural steroid injection in patients with spinal stenosis. The study has been criticized that, on the basis of the study protocol, these conclusions may lead to confusion, rather than clarification (171). Further, patients received epidural steroid injections once a week in a series of 3 for 3 weeks, and the injections were performed without fluoroscopic guidance, using an interlaminar ap-

proach, and were performed by 3 anesthesiologists from a single pain management clinic. Campbell et al (150) did not describe the volume of injectate nor the site of the injection. Further, routinely 3 epidurals were performed without any consideration as to whether the prior injection provided any relief or not, or if the patient continued to have pain or not. There were also other deficiencies with the presentation of the data. Overall it appears that 40% of the patients did not require decompression. Thus, it could be considered as to be a success. Basically, Campbell et al (150) have demonstrated that epidural steroid injections performed blindly with an interlaminar approach in a series of 3 injections may still be effective. Consequently, the study illustrates that epidural steroids may be significantly effective in spinal stenosis if they are performed with the appropriate delivery of medication to the target site with a specific approach under fluoroscopy.

Table 11 shows the characteristics of the studies of lumbar interlaminar epidurals in managing spinal stenosis included in the evidence synthesis.

Table 11. *Characteristics of published studies of blind lumbar interlaminar epidural injections in managing spinal stenosis.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤ 6 mos. Long-term relief > 6 mos.
Cuckler et al 1985 (110) Randomized, double-blind trial	73 pts. with back pain due to either acute herniated nucleus pulposus or spinal stenosis of > 6 mos. Experimental: 42 Control: 3.1	Experimental: 80 mg (2 mL) of methylprednisolone + 5 mL of procaine 1%. Control group: 2 mL saline + 5 mL of procaine 1%.	Timing: 24 hrs and an average of 20 mos. Outcome measures: subjective improvement, need for surgery.	There was no significant short-term or long-term improvements between both groups.	Negative short-term and long-term relief
Wilson-MacDonald et al 2005 (125) Randomized, controlled trial	93 pts. with MRI evidence of a disc prolapse, spinal stenosis, or a combination. Pts. had lumbosacral nerve root pain which had not resolved within 6 wks minimum. 32 pts. with 18 in the epidural group and 14 in the control group had spinal stenosis only, whereas 3 pts. in the epidural group and 15 pts. in control group had a combined disc herniation and spinal stenosis.	Experimental: epidural injection of bupivacaine 0.5% (40 mg) with methylprednisolone 80 mg. Control: intramuscular injection of 0.5% (40 mg) bupivacaine with 80 mg methylprednisolone.	Timing: 6 wks, 24 mos. Outcome measures: Oswestry Disability index, pain relief.	In the first 5 wks after epidural injection a useful improvement in nerve root symptoms was seen.	Negative short- and long-term relief
Campbell et al 2007 (150) Observational study	84 patients with lumbar spinal stenosis.	Pts. received an epidural steroid injection once a week for 3 weeks performed without fluoroscopic assistance, using an interlaminar approach performed by 3 anesthesiologists from a single pain management clinic.	24-month follow-up being differentiated into patients requiring surgery and those not requiring surgery.	Spinal canal dimension is not predictive of success or failure of lumbar interlaminar epidural steroid injections in pts. with spinal stenosis. The results showed 50 pts. requiring surgical decompression and 34 pts. improved after epidural steroid injection; 3 injections performed blindly in a series were effective in approximately 40% of the pts. in avoiding surgery.	Short-term not available and long-term negative

Effectiveness

Of the 3 evaluations studying the effectiveness of blind lumbar interlaminar epidural injections in spinal stenosis, none were shown to be positive for short-term or long-term relief.

Table 12 shows the results of 3 studies evaluating the effectiveness of blind lumbar interlaminar epidural injections in managing chronic low back or lower extremity pain of spinal stenosis.

Chronic Low Back Pain of Discogenic Origin without Radiculitis or Disc Herniation

There were no randomized trials in the evaluation of low back pain without disc herniation or radiculitis.

However, there was one observational study available evaluating the effect of spinal steroid injections for degenerative disc disease under fluoroscopy, which included intradiscal injections as well as interlaminar epidural injections (148). Epidural steroid injections were performed in 93 patients with degenerative disc disease and inflammatory endplate changes and in 139 patients without inflammatory endplate changes. The patients with inflammatory endplate changes (n = 78) or without inflammatory endplate changes (n = 93), all of whom were considered fusion candidates, underwent discography with or without intradiscal steroid in a randomized fashion. Pain and function were prospectively determined by a self-administered outcome survey (VAS pain, ODI, pain diagram [PD], and opinion of success) before and after the patients' injections for a 2-year follow-up. MRI and discography results were correlated with patient outcome scores. Patients received either interlaminar or transforaminal epidural steroid injections, all of which were performed under fluoroscopy; however, the proportion of patients receiving interlaminar epidural steroid injections is not described. However, this study over a period of 2 years had an extensive dropout rate of 60%. Ultimately, at 2 years, 49 of the 139 patients (35%) in this group had undergone a fusion. Of the patients who had implemented endplate changes (n = 93), approximately one-half of the patients expressed a positive opinion as to whether the epidural steroid injection was successful in the treatment of their symptoms during the first 3 months. Over subsequent follow-up periods, the success rate declined. The use of pain medication was found generally to have decreased during follow-up periods. The outcome scores for pain and disability showed significant improvement for back and leg pain (VAS and pain drawing) ($P < 0.001$).

Of the 139 patients who did not have inflammatory endplate changes and were treated with epidural steroid injections, 98 had not changed treatment after 3 month follow-up. Patients' self assessment of success slowly declined over time so that after one year, only 32 of the original 139 patients in this group considered their injection therapy to have been successful. However, a significant improvement in all outcome scales was found at all follow-up periods for those patients who did not drop out ($P < 0.001$).

A comparison of the 2 epidural steroid groups (inflammatory versus non-inflammatory endplates) revealed greater improvement for ODI scores for the

Table 12. *Results of published studies of effectiveness of blind lumbar interlaminar epidural steroid injections in managing spinal stenosis.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief				Results	
				< 3 mos.	3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 mos.	Long-term relief > 6 mos.
Cuckler et al 1985 (110)	RA,DB	60	37	NSD	NSD	NSD	NSD	N	N
Wilson-MacDonald et al 2005 (125)	RA	68	32	SI	NSD	NSD	NSD	P	N
Campbell et al 2007 (150)	O	53	84	NA	NA	NA	40%	NA	N

RA = randomized; DB = double blind; O = observational; C = control; T = treatment; SI = significant improvement; NSD = no significant difference; P = positive; N = negative; NA = not available

patients with inflammatory endplates at one to 3 and 4 to 6 month follow-up periods and pain drawing at the 4 to 6 month follow-up period. In addition, epidural steroid injection patients in the subgroup without inflammatory endplates were found to be using less pain medication in the early post treatment period. In addition, dropout rates were greater, although not significantly, for those without inflammatory endplates at all follow-up periods. The authors concluded that patients may have short-term benefit by epidural steroid injection without disc herniation or stenosis. Overall, 25% to 35% of patients with chronic low back pain resulting from degenerative disc disease had improved pain and function after epidural steroid injection at 2-year follow-up.

Effectiveness

Only one observational study (148) showed moderate results with short-term positive results and with negative long-term results in patients with chronic low back pain of discogenic origin without radiculitis or disc herniation.

Cost Effectiveness

In evaluations of cost effectiveness, Manchikanti et al (176) and Price et al (177) concluded that interlaminar epidural steroid injections were not cost effective.

Level of Evidence

The evidence-based on USPSTF criteria (105) is Level II-2 for blind lumbar interlaminar epidural injections for short-term relief in managing chronic low back and lower extremity pain secondary to lumbar disc herniation and/or radiculitis. The evidence is Level III for blind lumbar interlaminar epidural injections in managing low back pain of spinal stenosis, and chronic low back pain of discogenic origin without disc herniation or radiculitis.

Recommendations

Based on Guyatt et al's criteria (106), the recommendation for disc herniation and radiculitis for blind lumbar interlaminar epidural injections is 1C, a strong recommendation which may change when higher quality evidence becomes available for short-term relief. However, for long-term relief, the recommendation is 2B, with weak recommendation, with best action differing depending on circumstances or patients' or societal values. For spinal stenosis and discogenic pain without disc herniation and radiculitis, the evidence is Level III with 2C/weak recommendation, other alternatives may be equally reasonable.

Complications

The common complications of interlaminar epidural injections are of 2 types: those related to the needle placement, and those related to drug administration (1,58,59,147,163-171,178). Infectious complications include epidural abscess, meningitis, and osteomyelitis/discitis. Epidural hematomas are potentially the most serious of the epidural injection complications. Epidural hematomas can develop spontaneously even in patients with no evidence of any bleeding tendency, anticoagulation, or traumatic needle insertion. Neurological injuries are an uncommon complication that can occur when performing lumbar epidural steroid injections. Other complications include increased pain, seizures, chemical meningitis, dural puncture, subdural air, pneumocephalus, transient blindness, retinal necrosis, chorioretinopathy, hiccups, flushing, and arterial gas embolism (178-194). Side effects related to the administration of steroids are generally attributed either to the chemistry or the pharmacology of the steroids (195-199). The major theoretical complications of corticosteroid administration include suppression of pituitary adrenal axis, hypercorticism, Cushing's syndrome, osteoporosis, avascular necrosis of the bone, steroid myopathy, epidural lipomatosis, weight gain (200), fluid retention, and hyperglycemia.

The most commonly used steroids in neural blockade in the United States, methylprednisolone acetate, triamcinolone acetamide, and betamethasone acetate and phosphide mixture, have all been shown to be safe at epidural therapeutic doses in both clinical and experimental studies. It has been shown that at therapeutic doses of epidural steroids administered, complications were not noted (199).

Finally, radiation exposure is also a potential problem with damage to eyes, skin, and gonads (201-204).

Discussion

This systematic review of blind lumbar interlaminar epidural injections in managing chronic low back pain and lower extremity pain of disc herniation or radiculitis showed an indicated evidence of Level II-2 for short-term relief with evidence lacking with Level III for long-term relief. The evidence is lacking with Level III for spinal stenosis and discogenic pain. We have not evaluated the evidence for lumbar post-

laminectomy syndrome as this is not a commonly performed procedure and is considered unsafe with an interlaminar approach. The recommendation provided for short-term relief in disc herniation, based on Guyatt et al's (106) criteria is 1C/strong recommendation which may change when higher quality evidence becomes available for short-term management for patients with lumbar disc herniation and radiculitis. The recommendation is 2B/weak recommendation for long-term management of patients with disc herniation and radiculitis, with best action differing depending on circumstances or patients' or societal values. For low back and lower extremity pain secondary to spinal stenosis and disc degeneration without disc herniation or radiculitis, the recommendation is 2C/very weak recommendation, where other alternatives may be equally reasonable.

In addition to the paucity of available literature meeting inclusion criteria, all of the included studies followed flawed methodology without target delivery of steroids, delivering them without fluoroscopy, performing the procedures frequently between L3/4 and occasionally L4/5 in the lateral position, with poor assessment of outcomes application and analysis. The disadvantages of this approach without fluoroscopy include dilution of the injectate, extra epidural placement of the needle, intravascular placement of the needle, preferential cranial flow of the solution, preferential posterior flow of the solution, difficult placement (with increased risks in post-surgical patients), difficult placement below L4-L5 interspace, deviation of needle to non-dependent side, dural puncture, and trauma to spinal cord. There was a paucity of literature in the evaluation of spinal stenosis, whereas there was only one observational study available in evaluating chronic discogenic pain without disc herniation or radiculitis.

The ultimate results of this systematic review are similar to previous systematic reviews and guidelines. However, in this evaluation we attempted to evaluate the evidence separately for disc herniation and radiculitis, spinal stenosis, and chronic discogenic pain, whereas others have evaluated by combining multiple conditions and multiple techniques (caudal and transforaminal) into one category. In addition, in this study we have expanded the definition of short-term relief to 6 months or less, whereas long-term relief is defined as longer than 6 months –– a robust measure. Even then, the results were only positive for short-term relief for disc herniation and radiculitis, whereas they were negative or inconclusive for all other conditions and for long-term relief for disc herniation and radiculitis.

The evidence here is inferior compared to caudal epidural with or without steroids (95,96). Further, when the injections were performed under fluoroscopy, caudal epidurals showed superior results (88-91) in all conditions, including discogenic pain without disc herniation, spinal stenosis, and post surgery syndrome. Even blind injections showed superior results with cervical epidurals in the management of chronic neck pain. One of the reasons may be that the target delivery of steroids is much easier in the cervical epidural space than in the lumbar epidural space (74,95,205,206). Thus, the results of this evaluation with all flawed evidence, even though it looks appropriate based on the methodologic quality assessment, may not be utilized in contemporary clinical practice of interventional pain management.

Target site concentration of the administered drug including steroids depends on multiple injection variables including the route of administration. Interlaminar epidural injections are considered to be non-specific. Steroids may be prevented from migrating from the posterior epidural space to the anterior or ventral epidural space by the presence of epidural ligaments or scar tissue, with interlaminar administration. The extra epidural placement of the needle, which may go unrecognized without fluoroscopic guidance, is of paramount importance with the interlaminar approach (147,163-171). Other disadvantages of the interlaminar approach include erroneous placement of the needle, which may miss the targeted interspace without fluoroscopic guidance; preferential cranial flow of the solution in the epidural space; deviation of the needle to the non-dependent side; difficulty entering the epidural space and delivery of injectate below L5, for S1 nerve root involvement; potential risk of dural puncture and post-lumbar puncture headache; and finally, the rare, but serious risk of spinal cord trauma (147,163-171). It is a well-known fact that disc herniation mostly involves L4-L5 and L5-S1 discs and the preferential flow to higher levels by placing the needle at L3-4 obviates the entire philosophy of target delivery. Advocates of fluoroscopic guidance point to several studies which have shown that in as many as 30% of the lumbar epidural injections by experienced injectionists, the epidural space was misidentified (147,163-169). In fact, Botwin et al (169) in their prospective evaluation of epidurography con-

trast patterns in fluoroscopically guided lumbar interlaminar epidural injections found that dorsal contrast spread occurred in all patients, whereas ventral spread was present in only 36% of the patients. In addition, they also showed that the mean number of vertebral levels of cephalad spread was 1.28 and caudal spread was 0.88. In another study (170), the spread was unilateral 45% of the time and the contrast spread was anterior only 43% to 51% of the time based on the needle position, indicating over 49% of the time it was posterior.

The results of this systematic review are similar to previous systematic reviews and guideline syntheses (1,45-52). However, while some previous reviews (1,58,70) evaluated the evidence based on the route of administration — namely caudal, transforaminal, or lumbar interlaminar, others (62,65,66) have evaluated by combining multiple conditions and multiple techniques into one category, invariably leading to wrong conclusions (71,72,207). Further, in this study we have expanded the definition of short-term relief to 6 months or less, whereas long-term relief is defined as longer than 6 months, providing robust evidence. In addition, this is the first systematic review of the effectiveness of lumbar interlaminar epidural steroid injections as a separate category for lumbar interlaminar, spinal stenosis, and discogenic chronic low back pain.

The debate concerning caudal epidural steroid injections has been nurtured since the 1970s (1,58,59,62,65,66,70). The first systematic review of the effectiveness of caudal epidural steroid injections was performed by Kepes and Duncalf in 1985 (61). They concluded that the rationale for epidural and systematic steroids was not proven. However, in 1986, Benzon (73), 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. Thus, this illustrates that systematic reviews can be, and have been, providing different results based on the evaluators. More recently, ACOEM guidelines (68,69) provided negative evidence for lumbar interlaminar epidural injections. The debate concerning epidural steroid injections took center stage in the 1980s and 1990s with multiple publications (59,63). Bogduk et al (59) extensively studied interlaminar, caudal, and transforaminal epidural injections, including all the literature available at the time, and concluded that the balance of published evidence supports the therapeutic use of caudal epidurals. In 1995, Koes et al (62) reviewed 12 trials of lumbar and caudal epidural steroid injections and reported positive results from only 6 studies. However, a review of their analysis showed that there were 5 studies for caudal epidural steroid injections and 7 studies for lumbar epidural steroid injections and 5 of the 7 studies for lumbar interlaminar were negative. Their updated analysis (63) with the inclusion of 15 trials also arrived at the same conclusions. Multiple other investigators (62,65,66) also have provided differing conclusions, all negative. In general, criticism against systematic reviews in the past has been directed toward methodology, small size of the study populations, and other limitations, including long-term follow-up and outcome parameters on the available literature. Further, paucity of literature has been a factor in the systematic evaluation of evidence for the effectiveness of epidural injections.

Conclusion

This systematic review of blind lumbar interlaminar epidural injections in managing chronic low back pain and lower extremity pain of disc herniation or radiculitis showed an indicated evidence of Level II-2 for short-term relief with lacking of evidence with Level III for long-term relief and lacking of evidence with Level III for short- and long-term relief for spinal stenosis and discogenic pain. Caution must be exercised in the interpretation of these findings as all the studies included in this evaluation are blind interlaminar epidural injections and do not represent contemporary interventional pain management practice.

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