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Systematic Review

Systematic Review of Therapeutic Lumbar Transforaminal Epidural Steroid Injections

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Background: Epidural injection of corticosteroids is one of the most commonly used interventions in managing chronic spinal pain. The transforaminal route to the lumbar epidural space for steroid injection has gained rapid and widespread acceptance for the treatment of lumbar and leg pain. However, there are few well-designed randomized, controlled studies to determine the effectiveness of epidural injections. The role and value of transforaminal lumbar epidural steroid injections is still questioned.

Study Design: A systematic review of transforaminal epidural injection therapy for low back and lower extremity pain.

Objective: To evaluate the effect of transforaminal lumbar epidural steroid injections in managing lumbar (low-back) and sciatica (leg) pain.

Methods: The available literature of lumbar transforaminal epidural injections in managing chronic low back and lower extremity pain was reviewed. The quality assessment and clinical relevance criteria utilized were the Cochrane Musculoskeletal Review Group criteria as utilized for interventional techniques for randomized trials and the criteria developed by 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).

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 the bibliographies of known primary and review articles.

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 indicated evidence is Level II-1 for short-term relief and Level II-2 for long-term relief in managing chronic low back and lower extremity pain. .

Limitations: The limitations of this systematic review include the paucity of literature.

Conclusion: The indicated evidence for transforaminal lumbar epidural steroid injections is Level II-1 for short-term relief and Level II-2 for long-term improvement in the management of lumbar nerve root and low back pain.

Key words: Spinal pain, chronic low back pain, lower extremity pain, transforaminal epidural steroids, radiculopathy, sciatica, steroids, local anesthetic

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It is estimated that 20% of the general population may suffer from chronic pain of any type at a given point in time (1). Spinal pain may be the most common type of chronic pain suffered and has a reported lifetime prevalence of 54 – 80% (2-10). The economic and social toll of chronic spinal pain and its consequences are great and represent a significant health problem.

Kuslich et al (11) identified intervertebral discs, facet joints, ligaments, facia, muscles, and nerve root dura as tissues capable of transmitting pain in the low back. In the American literature, Mixter and Barr (12) were the first to create widespread interest in the disc as a source of pain with publication of their 1934 hallmark description of the herniated nucleus pulposus. Still today, the pathophysiology of spinal radicular pain is the subject of ongoing research and controversy. In addition to the mechanical component, inflammation of the compressed nerve root is an important factor in the pathophysiology of radicular and discogenic pain (13-21).

Epidural injections for managing chronic low back pain are one of the most commonly performed interventions in the United States (22-33). However, there are several approaches available to access the lumbar epidural space; transforaminal, caudal, and interlaminar (22,32,33).

Substantial differences have been described between these 3 approaches, with the transforaminal approach having the advantage of being target specific and using the smallest volume, fulfilling the aim of reaching the primary site of pathology, namely the ventrolateral epidural space (34-39). Abdi et al (32) showed that the evidence of lumbar transforaminal epidural steroid injections for lumbar nerve root pain was strong for short-term (< 6 weeks) and moderate for long-term improvement (> 6 weeks). However, they showed limited evidence for transforaminal injections for lumbar radicular pain in post surgery syndrome. Boswell et al (22) also used the same evidence in the development of interventional pain management guidelines. DePalma et al (38) showed that there was moderate evidence in support of selective nerve root blocks in treating painful radicular syndromes.

European guidelines for the management of chronic non-specific low back pain (39) also provided a favorable level of evidence for transforaminal epidural steroids injections. However, multiple other reviews have shown no significant evidence for transforaminal epidural injections as a therapeutic modality (40,41). In a reassessment of the evidence synthesis of occupational medicine practice guidelines for interventional pain management, Manchikanti et al (28,42) showed Level 1 evidence for both short-term relief (6 months or less) and long-term relief (longer than 6 months). Nevertheless, the most effective and beneficial route for the administration of epidural steroids remain controversial; and neither the effectiveness nor the superiority of transforaminal epidural injections has been proven clearly. Further, the underlying mechanism of action of epidurally administered steroid and local anesthetic injections is still not well understood. In addition, a new treatment has been proposed with intraforaminal injection of oxygen-ozone (02-03) (43,44). In fact, this new evidence has shown better relief with the oxygen-ozone combination, than with steroids (43-46).

This systematic review is undertaken to evaluate transforaminal lumbar epidural injections with or without steroids.

Methods

Literature Search

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

The search strategy emphasized chronic low back and lower extremity pain with a focus on lumbar transforaminal epidural injections. Search terminology included lumbar intervertebral disc, disc-related pain, sciatica, lumbar transforaminal epidural injections, lumbar selective nerve root blocks, or lumbar radicular pain.

Selection Criteria

The review focused on randomized trials, observational studies, and reports of complications. The population of interest was patients suffering with chronic low back and lower extremity pain for at least 3 months. Only lumbar transforaminal epidural injections with or without steroids were evaluated. All of the studies providing appropriate management and 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.

Review Criteria

Studies were selected if they met the inclusion criteria.

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) (47) for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) quality criteria for assessment of observational studies (Table 2) (48) with consensus-based weighted scoring developed by the guidelines committee of the American Society of Interventional Pain Physicians (ASIPP) utilized in multiple evaluations (28,49-53).

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

Clinical Relevance

Clinical relevance of the included studies was evaluated according to 5 questions recommended by the Cochrane Back Review Group (27,54).

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.

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 (47).

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 (48).

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 (27).

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) (61).

In the recent Cochrane review of "Injection Therapy for Subacute and Chronic Low Back Pain" (27) the authors considered 20% improvement in pain scores (55) and 10% improvement in functioning outcomes (56) 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 (27) and others have considered 6 weeks as short-term and longer than 6 weeks as long-term. We also utilized methodologic quality assessment criteria (27) for minimum inclusion, thus this current 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, but included only quality observational studies with scores of 50 or more on a scale of 0 – 100 based on the AHRQ criteria. This inclusion improves the generalizability of the systematic review and the intervention to the population (57-60).

Analysis of Evidence

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 (61) developed by the U.S. Preventive Services Task Force (USPSTF).

Recommendations

Grading recommendations were based on Guyatt et al's criteria as illustrated in Table 5 (62).

Outcome of the Studies

In the randomized trials, a study was judged to be positive if the transforaminal epidural injection therapy was clinically relevant and effective, either with a placebo control or active control. This indicates that the difference in effect for primary outcome measure was statistically significant on the conventional 5% level. In a negative study, no difference between the study treatments or no improvement from baseline was identified. 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. However, observational studies were only included in the evidence synthesis if there were less than 4 randomized trials meeting inclusion criteria for evidence synthesis.

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 (62).

Results

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

Our search strategy yielded multiple manuscripts evaluating the effectiveness of lumbar transforaminal epidural injections with or without steroids (43-45,63-101).

Methodologic Quality Assessment

Randomized Trials

Of the 11 randomized trials, 7 studies met the inclusion criteria (45,68,72,83,90,92,94). Four studies were excluded from the analysis for short-term follow-up and other deficiencies (43,73,89,94). Even though follow-up was adequate, Gallucci et al (43) was excluded because intradiscal injections were combined with transforaminal epidurals, thus negating the individual effect to be evaluated.

Methodological quality assessment criteria are illustrated in Table 6. There were 2 studies with duplicate presentations: Riew et al (83,94) and Karppinen et al (72,90). Thus, methodologic quality assessment was carried out for a total of 5 studies (45,68,72,83,90,92,94) with scores ranging from 44 to 86. The study by Devulder (68) with a score of 44 failed to meet the methodologic quality assessment criteria.

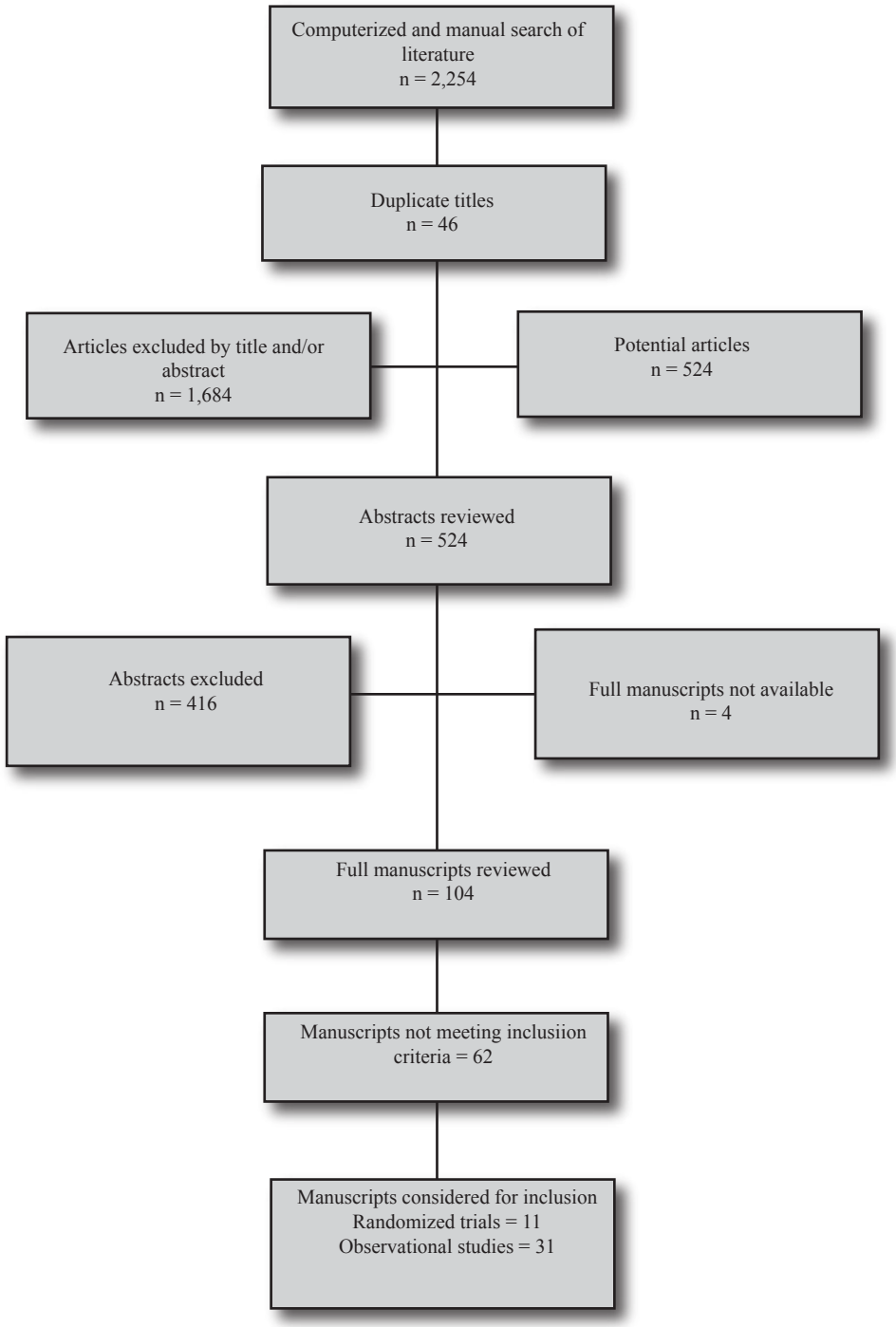

Fig. 1. *The flow diagram illustrating published literature evaluating lumbar transforaminal lumbar epidural injections.*

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

CRITERION		WEIGHTED SCORE (points)	Riew et al (83,94)	Devulder (68) *	Vad et al (92)	Karppinen et al (72,90)	Jeong et al (45)
Study population							
A	Homogeneity	2	2	2	2	2	2
B	Comparability of relevant baseline characteristics	5	5	5	3	5	5
C	Randomization procedure adequate	4	4	4	1	4	4
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	2
	< 10% loss for follow-up	2	2	2	2	2	2
F	> 50 subject in the smallest group	8	—	—	—	8	—
	> 100 subjects in the smallest group	9	—	—	—	—	—
Interventions							
G	Interventions included in protocol and described	10	10	10	10	10	10
H	Pragmatic study	5	5	5	5	—	5
I	Co-interventions avoided or similar	5	5	5	5	5	5
J	Placebo-controlled	5	—	—	—	5	—
Effect							
K	Patients blinded	5	5	1	—	5	5
L	Outcome measures relevant	10	10	2	10	10	10
M	Blinded outcome assessments	10	5	1	5	10	—
N	Follow-up period adequate	5	5	2	5	5	5
Data-presentation and analysis							
O	Intention-to-treat analysis	5	5	—	5	5	—
P	Frequencies of most important outcomes presented for each treatment group	5	5	—	5	5	5
	TOTAL SCORE	100	73	44	63	86	63

* Failed to meet exclusion criteria. 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 (47).

Only 2 of the 4 studies had groups of patients greater than 50 participants (45,72,90). Only one study was placebo-controlled (72,90). However, the placebo solution in this study was injected over the nerve root as in the intervention group with local anesthetic and steroid. This may not be considered as a true placebo control as we are not aware of the effects of the injection of sodium chloride solution into the epidural space or over the nerve roots. The patients were not blinded in one of the studies (92). Three (72,83,90,92,94) of the 5 studies included an intention to treat analysis.

Clinical Relevance Assessment

All 4 of the included studies met clinical relevance criteria (45,72,83,90,92,94). Clinical relevance criteria was evaluated as shown in Table 7 for 4 randomized trials.

Study Population

The populations evaluated in the 4 studies were consistent in that they included both back and leg pain patients and evidence of nerve root compression on imaging studies. Some studies did exclude patients with prior lumbar spine surgery, while the others did not (83,94).

Table 7. *Clinical relevance of randomized clinical trials evaluating the effectiveness of lumbar transforaminal epidural injections.*

	Riew et al (83,94)	Vad et al (92)	Karppinen et al (72,90)	Jeong et al (45)
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	5/5	5/5	5/5	5/5

+ = positive; - = negative

Scoring adapted from Staal JB et al. Injection therapy for subacute and chronic low-back pain. Cochrane Database Syst Rev 2008; 3:CD001824 (27).

Cost Analysis

Only Karppinen mentioned any kind of cost analysis (72). At the 4-week follow-up period the patients who received methylprednisolone transforaminally utilized fewer therapy visits and less drugs resulting in significantly lower costs. At all other times there was no significant cost difference in the groups. No other study performed any kind of cost analysis.

Observational Studies

After methodologic quality assessment, 4 randomized trials met the inclusion criteria for evidence synthesis, thus observational studies were not evaluated for methodologic assessment quality criteria or evidence synthesis.

Study Characteristics

Table 8 illustrates the details of the randomized trials studying the effectiveness of lumbar transforaminal epidural steroids injection.

Jeong et al (45) essentially compared transforaminal epidural injections to themselves and only altered the level (preganglionic vs. ganglionic) injected. The question they sought to answer was where it is best to inject; at the site where the disc is contacting the presumed affected nerve or at the foramen where that nerve exits. If a patient has a disk herniation at L4-5 that contacts the L5 nerve root then one could perform a pre-ganglionic injection at the L4-5 foraminal level or a ganglionic injection at the L5-S1 level. Jeong's group performed 239 transforaminal injections, 127 ganglionic and 112 pre-ganglionic. The drugs injected were triamcinolone and bupivacaine. They did assess patient reported pain scores and degree of improvement. At the short-term the pre-ganglionic injection group did better than the ganglionic group. At long-term follow-up there was no statistically significant difference between the groups but a majority of the patients in both groups rated their outcomes as good to excellent (79% at short-term and 63.9% at long-term). The authors concluded that the implication for patient care is that a pre-ganglionic approach may be considered an alternative to a ganglionic approach when the needle tip cannot be advanced adjacent to the neuroforamen or adequate amounts of the drug cannot be injected into the epidural space through the neuroforamen owing to severe neuroforaminal stenosis. However, the use of transforaminal epidural steroids injection with a pre-ganglionic (99 of 112 patients) approach is more effective than a ganglionic (90 of 127 patients) approach at short-term follow-up and is almost as effective (64 of 106 patients) as a ganglionic approach (78 of 116 patients) at mid-term follow-up.

Karppinen et al evaluated transforaminal epidural steroid injections in patients with sciatica (90). Eighty patients received transforaminal epidural injections of methylprednisolone and bupivacaine and another 80 received saline injections via a transforaminal injection. Pain and Oswestry scores were recorded. Both groups showed improvement with the steroid group doing better than the saline at 2 weeks and the saline group doing better at the 3 and 6 month points. Interestingly, the steroid and local anesthetic infiltration seemed to be associated with a rebound phenomenon at 3 and 6 months. This was manifested by little or no improvement in pain and disability between 3 and 6

Table 8. *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 mos Long-term relief > 6 mos
Karppinen et al 2001/2001 (72,90) Randomized, double-blind trial	160 consecutive, eligible pts with sciatica with unilateral symptoms of 1 to 6 mos. duration. None of the pts had undergone surgery.	Experimental: local anesthetic and methylprednisolone. Control: normal saline.	Timing: 2 wks, 4 wks, 3 mos., 6 mos., and 1 yr. Outcome measures: Pain relief, sick leave, medical costs, and future surgery. A subgroup analysis and cost effectiveness was performed (309). For the cost-effectiveness estimate, the total costs were divided by the number of responders.	Steroid injection produced significant treatment effects and short-term improvement in leg pain, straight leg raising, disability, and in Nottingham Health Profile and emotional reactions. In the subgroup analysis for contained herniations, the steroid injection produced significant treatment effects. By one-year, steroid seemed to have prevented operations for contained herniations, costing $12,666 less per respondant in the steroid group ($P < 0.01$).	Positive short-term relief and negative long-term relief. For contained herniations and lesions at L3-L4-L5, steroid treatment also prevented surgery for contained herniations. However, steroid was counter effective for extrusions.
Riew et al 2006/2000 (83,94) Prospective, randomized, controlled, double-blind study	55 pts with lumbar disc herniations or spinal stenosis referred for surgical evaluation. 28 pts. in experimental group (bupivacaine and betamethasone) and 27 pts. in control group (bupivacaine only).	Experimental: transforaminal nerve root or epidural steroid injection with 1 mL of 0.25% bupivacaine and 6 mg of betamethasone Control: 1 mL of 0.25% bupivacaine. As many as 4 injections were given during the follow-up.	Initial outcomes were evaluated at one-year. Injection was considered as a failure if the patient opted for operative treatment. North American Spine Society questionnaire also used.	Of the 55 randomized pts, 29 avoided surgery at one-year. Twenty-one of 29 were re-evaluated. Seventeen of the 21 pts. still had successful results with no operative intervention after 5 yrs.	Positive short-term and long-term relief.
Vad et al 2002 (92) Prospective, randomized trial	Patients with leg pain, with documented herniated nucleus pulposus or manifested clinical signs such as radicular pain with lumbar radiculopathy.	Experimental: betamethasone 9 mg, and 2% preservative-free Xylocaine (1.5 mL) per level. Control: trigger point injections.	Timing: 3 wks, 6 wks, 3 mos., 6 mos., and 12 mos. Outcome measures: Roland-Morris score, visual numeric score, finger-to-floor distance, patient satisfaction score.	Group receiving transforaminal epidural steroid injections had 84% success rate compared with 48% for group receiving trigger point injections.	Positive short-term and long-term relief.
Jeong et al 2007 (45) Prospective randomized controlled study	239 consecutive pts were randomly assigned to either the ganglionic group or pre-ganglionic group, with 2 different types of injections for pts with radicular pain meeting the inclusion criteria of the presence of lumbosacral radiculopathy, clear documentation of nerve root compression with either subarticular or paracentral disc herniation by using clinical and cross sectional imaging studies, following inclusion criteria. Patients were divided into 2 groups by duration of pain with less than 6 months and more than 6 months. 46 pts in the ganglionic group and 49 pts in the pre-ganglionic group had pain for longer than 6 months.	Patients were randomized to receive either the ganglionic or the pre-ganglionic transforaminal epidural steroid injection at one level. The pts in the ganglionic group underwent transforaminal epidural steroids injection at the location of the exiting nerve root, whereas in the pre-ganglionic group, they underwent the injection at the supra-adjacent intervertebral disc level and each one received 0.5 mL of bupivacaine hydrochloride and 40 mg of 1 mL of triamcinolone acetonide.	All pts underwent outcomes at 1-month and after 6 months, which included visual analog scale (VAS) and a 4-grade scale with regard to degree of improvement, excellent, good, fair, or poor. They considered 50% or greater in VAS along with a self-reported good to excellent improvement as an effective treatment.	Short-term and mid-term follow-up. Mid-term follow-up was carried out after 6 mos., only 17 pts were lost to mid-term follow-up. Mean interval of mid-term follow-up as 373 days ranging from 216 to 547 days. Results showed that the pre-ganglionic group had a better treatment effect than did the ganglionic group, however there were no significant differences identified at mid-term follow-up.	Positive short-term relief with both techniques. There was no long-term follow-up available, even though it is implied.

months but then equal pain and disability scores at 12 months. Karppinen et al (72) in their subgroup analysis of the randomized trial (90) showed significantly positive results for contained herniations at one-year.

Riew et al (83,94) evaluated whether selective nerve root injections might help patients with lumbar radicular pain to avoid spine surgery. Fifty-five patients who were deemed surgical candidates were treated and randomized to receive either a selective nerve root injection of betamethasone 6 mg with bupivacaine or a selective nerve root injection of bupivacaine alone. The patients were allowed up to 4 injections of the same study medicine during the evaluation. The patients were followed for between 13 and 28 months. There was no set follow-up evaluation at a short- or long-term point. At the end of the period, 18 of the 27 patients receiving only bupivacaine had chosen to undergo surgery. Of the 28 patients receiving the combination of betamethasone and bupivacaine, only 8 had undergone surgery. The difference was highly significant. In the follow-up study, Riew et al (83) showed positive long-term results with or without steroids.

Vad et al (92) studied the effect of transforaminal epidural betamethasone 9 mg and lidocaine and compared it to a lumbar paraspinal muscle trigger point injection of saline. Forty-eight patients were included. Outcomes included pain score, patient satisfaction, and other measures of function. The patients were followed for an average of 1.4 years but no set short- or long-term follow-up evaluations were scheduled. Patients improved in both groups but the transforaminal group did significantly better with a much lower pain score at the end and a larger percentage of patients (84% vs. 48%) achieving a successful outcome in a shorter period of time than the trigger point group (6 weeks vs. 12 weeks).

Effectiveness

Of the 4 randomized trials evaluating lumbar transforaminal epidural steroid injections, all showed positive results for short-term relief (45,72,83,90,92,94), 2 were positive for long-term relief (83,92,94), the results of long-term relief were not available for one study (45), whereas one was negative (72,90).

Table 9 illustrates results of effectiveness of lumbar transforaminal epidural steroid injections.

Level of Evidence

The indicated evidence for lumbar transforaminal epidural steroid injections is Level II-1 for short-term relief and Level II-2 for long-term relief in managing chronic low back and lumbar nerve root pain based on USPSTF criteria.

Recommendations

Based on Guyatt et al's criteria (62), the recommendation for lumbar transforaminal epidurals is 1C/strong recommendation, moderate or low quality evidence, with a caveat that the recommendation may change when higher quality evidence becomes available.

Table 9. *Results of randomized trials of effectiveness of lumbar transforaminal epidural injections.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief			Results	
				3 mos	**6 mos**	**12 mos**	**Short-term relief ≤ 6 months**	**Long-term relief > 6 months**
Karppinen et al 2001/2001 (72,90)	RA, DB	81	C = 80 T = 80	SICH	NSI	NSI	P	N
Riew et al 2006/2000 (83,94)	P, RA, DB	68	55	NA	NA	33% vs. 71% (avoided surgery)	P	P
Jeong et al 2007 (45)	RA, DB	63	239	PG 99 of 112 G 90 of 127	PG 64 of 106 G 78 of 116	NA	P	NA
Vad et al 2002 (92)	RA	58	48	NA	NA	48% vs. 84%	P	P

P = prospective; RA = randomized; DB = double blind; C = control; *T = treatment;* PG = pre-ganglionic; G = ganglionic; SICH = significant improvement in contained disc herniation; *NSI = no significant improvement; vs. = versus*; *NA = not available; P = positive; N = negative.*

Complications

The most common and worrisome complications of transforaminal epidural steroid injections in the lumbar spine, though rare, are related to neural trauma, vascular trauma, intravascular injection, and infection (35,64,102-120).

Botwin et al (64) reported complications in 207 patients receiving 322 transforaminal lumbar epidural steroid injections. Complications included transient headaches in 3.1%, increased back pain in 2.4%, increased leg pain in 0.6%, facial flushing in 1.2%, vasovagal reaction in 0.3%, increased blood sugar in 0.3%, and hypertension in 0.3%. The incidence of minor complications was 9.6% per injection with no major complications.

Furman et al (103) reported among the 761 transforaminal epidural steroid injections included in the study, the overall rate of intravascular injection was 11.2%, with a higher rate of intravascular injections (21.3%) at S1 transforaminal compared with those at the lumbar levels (8.1%).

Manchikanti et al (35) reported intravenous placement of the needle in 22% of the procedures. Other complications included pain during the injection with back pain in 43% of the patients and leg pain in 22% of the patients. Postoperative complications were reported in 34% of the patients with soreness at the injection site in 18%, increased pain in 5%, muscle spasms in 4%, swelling in 4%, headache in 3%, minor bleeding in 2%, dizziness in 1%, nausea and vomiting in 1%, fever in 1%, numbness in 1%, and voiding difficulty in 1%. Transforaminal injections have been reported with complications including spinal cord injury and infarction (104,105), paraplegia (106), and intracord injection (105).

Huston et al (107) reported no major complications noted and 91% of the patients had no side effects during the injection. The most common side effect noted was increased pain at the injection site after the injection, which was seen in 17.1% of the lumbar patients.

Side effects related to the administration of steroids are generally attributed either to the chemistry or to the pharmacology of steroids (108). The major theoretical complications of corticosteroid administration include the suppression of pituitary adrenal axis, hypocorticism, Cushing's syndrome, osteoporosis, avascular necrosis of the bone, steroid myopathy, epidural lipomatosis, weight gain, fluid retention, and hyperglycemia (109-117). Radiation exposure is also a potential problem with damage to eyes, skin, and gonads (118-120).

Discussion

This systematic review evaluating the effectiveness of lumbar transforaminal epidural injections in managing chronic radicular pain indicated Level II-1 or II-2 evidence, with a 1C/strong recommendation. Four randomized trials met the criteria for inclusion in this evaluation. The results of this systematic review are similar to the review by Abdi et al (32) and the reassessment of the American College of Occupational and Environmental Medicine (ACOEM) guidelines evidence by Manchikanti et al (28).

In 2008, Pearson et al (121) published their report assessing the effect of lumbar discectomy on patients with acute sciatica. The patients could be randomized into either the surgical group or the standard non-operative group. After randomization and surgery the patients were followed for up to 2 years. There was a 3 month follow-up assessment but no 6 month follow-up. They used a 6 point Likert-type scale to assess back pain "bothersomeness" as opposed to a standard numeric analog pain score. Looking at their data tables it is noted that the average back pain "bothersomeness" score for all groups is 3.9. Surgery reduced this score by 2.2 (56.4%) for all surgical patients. The non-operative group's pain "bothersomeness" score decreased by 1.3 (33%) in the same 3 months. After 3 months the scores in both groups essentially stabilized for the next 2 years. Their scores stayed roughly the same as at the 3 month mark, with a slight improvement in the non-operative group's score and a slight increase in the surgical group's score. The surgery group still had a better pain score at all time periods. In a second study, Mortimer and her colleagues (10) polled 790 patients with back pain that had sought care in any of several local clinics in Sweden. They did utilize a numerical pain score (0 – 100) and a disability score different from any used in the 8 transforaminal groups. They polled the patients by a mailed questionnaire at 6 months, 2 years, and 5 years. Four hundred and fifty-nine patients completed the study. The baseline median pain score was 47. At the 6 month mark the average pain score was calculated as 28.3, based on an average score of 30 for the 202 men and a score of 27 for the 257 women. This is a change of 18.7 points or 39% from baseline. The disability improved dramatically at 6 months, from an average score of 27 to 7, which is a 74% drop. In summary, disc surgery reduces the pain roughly the same amount as transforaminal lumbar epidural steroid injections as well as interlaminar and caudal epidurals at 3 months after treatment. The patients that received standard conservative therapy did about

the same as patients that received transforaminal saline or local anesthetic but not as good as those that received an epidural steroid injection of any kind or surgery. In the Mortimer study, at 6 months the patients' pain had decreased, on its own, by about 39%. This is less than the transforaminal steroid and transforaminal saline groups and about the same as the groups that received an interlaminar or caudal epidural steroid. Since Pearson et al's (121) surgery patients seemed to plateau at around 50% reduction in pain score, we could assume that surgical patients would also be better than Mortimer's patients at 6 months.

The current systematic review shows that transforaminal epidural steroid injections, when appropriately performed, should result in significant improvement. These procedures can reduce the patient's pain by 64% to 81%, disability by 60% to 63%, and depression by 56%. Considering the low risk and less expensive nature of the procedure, compared to surgical interventions, epidural injections with or without steroids seem to be cost effective (122-127).

With caudal and interlaminar epidurals, a common problem encountered is inaccurate needle placement, leading to inaccurate placement of the injectate. However, that is not an issue with transforaminal epidurals as it is required that transforaminal epidurals always be performed under fluoroscopy with contrast injection (128-132). Even then, there has been controversy with regards to the spread of the contrast with transforaminal epidural injections (35,36,89,127,133-135), showing a lack of ventral filling in some cases.

It appears that the underlying mechanism of action of epidurally administered steroid and local anesthetic is based on the belief that the achieved neural blockade alters or interrupts nociceptive input, the reflex mechanism of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities (109,136). Corticosteroids also have been shown to reduce inflammation by inhibiting either the synthesis or release of a number of pro-inflammatory mediators and by causing a reversible local anesthetic effect (109,136-145). The emerging evidence also shows that the long-lasting effect may be obtained with local anesthetics with or without steroids (88,146-164). In fact, in rat experiments of nerve root infiltration, Tachihara et al (145) illustrated that mechanical allodynia was prevented by local anesthetic with or without steroid, even though no additional benefit from using corticosteroid was identified. Thus, it is suggested that corticosteroids may be unnecessary for nerve root blocks. This concept has been reinforced by numerous randomized and observational studies (36,123-126,156,158,161-168).

The results of this systematic review may be applied in interventional pain management practices utilizing appropriate evaluations. Further, these results are also generalizable.

The limitations of this study include that we were able to find only 4 appropriately performed studies which met inclusion criteria and were clinically relevant. Further, methodologic criteria has been highly variable along with sample sizes. The studies were heterogenous.

The results of this systematic review have significant implications for clinical practice. Transforaminal epidural injections show a significant reduction of pain scores in patients with lumbar radiculitis when compared to doing nothing, conservative management without injection therapy, and probably lumbar interlaminar epidural injections (53). However, the differences between transforaminal and caudal epidural are not significantly different based on the recent systematic review of caudal epidural injections (51).

The future implications for research should include a clear case definition with consistent inclusion and exclusion criteria, clear outcome measures, appropriate design, and reporting of randomized trials (58,59,169-171).

Conclusion

The results of this systematic evaluation of lumbar transforaminal epidural injections showed that they have significant effect in relieving chronic pain of lumbar disc herniation and radiculitis with indicated evidence levels of Level II-1 to II-2 with a 1C/strong recommendation. However, evidence must be examined on a regular basis and the data needs to be updated if further evidence becomes available.

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