

Steroid for epidural injection in spinal stenosis: a systematic review and meta-analysis

Kuan Liu*
Pengcheng Liu*
Run Liu
Xing Wu
Ming Cai

Department of Orthopaedics,
Shanghai Tenth People's Hospital,
Tongji University School of Medicine,
Shanghai, People's Republic of China

*These authors contributed equally
to this work

Purpose: To investigate the effectiveness and safety of epidural steroid injections in patients with lumbar spinal stenosis (LSS).

Methods: We performed a search on the CENTRAL, Pubmed, Embase and Cochrane databases up to September 2014. We recovered 17 original articles, of which only 10 were in full compliance with the randomized controlled trial (RCT) criteria. These articles were reviewed in an independent and blinded way by two reviewers who were previously trained to extract data and score their quality by the criteria of the Cochrane Handbook (5.1.0).

Results: We accepted ten studies with 1,010 participants. There is minimal evidence that shows that epidural steroid injections are better than lidocaine alone, regardless of the mode of epidural injection. There is a fair short-term and long-term benefit for treating spinal stenosis with local anesthetic and steroids.

Conclusions: This meta-analysis suggests that epidural steroid injections provide limited improvement in short-term and long-term benefits in LSS patients.

Keywords: lumbar spinal stenosis, epidural injection, steroid, local anesthetic, chronic pain

Introduction

Lumbar spinal stenosis (LSS) is a degenerative disease that affects the lumbar spine. LSS can cause back and leg pain due to the compression of neuronal structures and intraspinal vasculature due to the narrowing of the spinal canal. LSS is quite common in people older than 65 years, and its most significant clinical symptom is intermittent neurogenic claudication. Neurogenic claudication is characterized by pain, paresthesia, and cramping in one or both legs.¹ It is caused suddenly by walking and prolonged standing and can be relieved through sitting and bending forward.^{2,3}

Neurogenic claudication is a main reason leading to disability and lost independence in the elderly population.⁴ The patients with symptomatic LSS not only suffer from back and leg pain, but are also at high risk for developing serious complications. Disability and lost independence may lead to physical deterioration and obesity, which may eventually lead to serious health problems.⁵ Those afflicted have more serious walking limitations than individuals with knee or hip osteoarthritis.⁶ Consequently, their restricted ability to walk and stand lead to a significant decrease in quality of life.⁷⁻⁹

The rate of surgery for LSS has risen dramatically, especially in the USA.^{10,11} Some good outcomes from surgery have been demonstrated, but the literature has also suggested limited long-term benefits when compared to nonsurgical management.^{12,13} Some conservative treatment is recommended prior to surgical intervention. Researchers have focused on the use of epidural steroid injections to treat pain due to LSS.¹⁴⁻²³

Correspondence: Xing Wu; Ming Cai
No 301 Middle Yanchang Road, Shanghai
Tenth People's Hospital, Shanghai,
200072, People's Republic of China
Email orthopedics_dsyy@126.com;
cmdoctor@tongji.edu.cn

Because pain and limited walking are the main impaired functions in patients with LSS, decreasing pain and improving walking ability are the primary goals for treatment.³ Two systematic reviews on epidural steroid injections for LSS are available.^{24,25} However, whether epidural steroid injections can relieve pain and improve walking ability in patients with LSS in short-term and long-term follow-ups is unclear. It is important to evaluate the role of epidural steroid injection treatments to manage patients with LSS. Therefore, we undertook a systematic review and meta-analysis of all the published literature to evaluate the effectiveness and safety of epidural steroid injection interventions for the treatment of LSS.

Materials and methods

We conducted this systematic review and meta-analysis according to the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions (Version 5.1.0; Oxford, UK).²⁶

Search strategy

The Cochrane library, Google Scholar, CENTRAL, Pubmed and Embase databases were searched independently by two investigators (KL and PCL), and relevant studies published before September 2014 were retrieved. The search strategy was based on a combination of the following medical subject headings (MeSH) and keywords: “steroid”, “spinal stenosis”, “pain”, “epidural injection”, and “local anesthetic”. No restriction to specific languages or years of publication were included. The “related articles” function was used to broaden the search. The reference lists of the selected studies were also examined manually to identify relevant studies that were not discovered during the database searches. The corresponding authors were contacted when additional information was needed.

Study selection

We included randomized controlled trials (RCTs) that evaluated the efficacy and safety of epidural injections of steroids plus local anesthetic versus local anesthetic alone for the treatment of LSS patients. The inclusion criteria for the systematic review and meta-analysis were as follows: (1) randomized controlled trials in adults with LSS with epidural injection treatment; (2) clinical or radiological diagnosis of LSS; (3) describe neurogenic claudication with back (leg) pain and gait assessment; (4) provide the dosage and route of epidural steroid injection administration; and (5) outcomes measured, such as walking ability, pain intensity, quality of life, and global improvement. Studies

evaluating radiculopathy caused by disc lesions were excluded. Studies with mixed populations were only included if the data for neurogenic claudication due to lumbar spinal stenosis were provided.

Outcome measures

All of the eligible studies were reviewed for baseline data (such as age and sex), intervention (such as epidural injection administration method, dose and duration) and outcome measures. Both subjective and objective functional outcome measurements were used to evaluate the data. However, the primary key pooled outcomes were the pain scale (such as visual analog scale [VAS]) and walking ability. Adverse effects of epidural steroid injections were also examined. The quality of eligible studies was also assessed according to the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0.

Quality assessment

The titles and abstracts of the publications were reviewed using the previously mentioned selection criteria by two readers (KL and PCL). The data extraction of all of the variables and outcomes of interest and assessment of the methodological quality were performed independently by two investigators. Any disagreement was resolved by discussion and consensus. The methodological quality of the trials was assessed using the Cochrane Handbook for Systematic Reviews of Interventions 5.1.0.

Statistical methods

Statistical analysis was performed by Review Manager 5.3.3 (Cochrane Collaboration, Nordic Cochrane Centre, Copenhagen, Denmark). For dichotomous variables, the relative risks (RRs) were measured with 95% confidence intervals (CIs), while the weighted mean difference (WMD) was measured with the 95% CIs for continuous variables. P -values <0.05 were considered statistically significant, and the 95% CIs are reported. Statistical heterogeneity among studies was evaluated by Q -statistic and quantified by the I^2 statistic. Both a fixed-effects model and a random-effects model were used to obtain summary RRs or WMDs. If the Q or I^2 statistic was significant, a random-effects model was used. Otherwise, a fixed-effects model was used. Funnel plots and the Egger test (with $P < 0.05$ considered statistically significant) were created to visually evaluate the presence of publication bias. A sensitivity analysis was also conducted, in which the RCTs were excluded to determine the stability of the combined RRs or WMDs.

Results

Literature search

The initial literature search retrieved 101 relevant articles, and duplicates were discarded. After a careful screen of the titles, 84 articles were excluded as they did not cover the topic of interest. After reviewing the abstracts, seven more articles were excluded (one editorial and six reviews), leaving ten studies for further full publication review. Therefore, ten studies matched the selection criteria and were suitable for meta-analysis,^{14–23} and all of them were prospective randomized control trials (Figure 1). A total of 1,010 patients (498 who received epidural steroid injection and 512 who received epidural local anesthetic injection) were enrolled in the studies. The key characteristics of the included studies are summarized in Table 1. All the studies involved patients with LSS and a follow-up of at least 6 weeks. Ten level I–II studies from 1985 to 2014 that compared epidural steroid injection with epidural local anesthetic injection for the treatment of

LSS prospectively and randomly were identified. On review of the data extraction, there was 100% agreement between the two investigators.

Figure 2 summarizes the methodological quality of the studies. All of the studies were RCTs with a high level of methodological quality. Thus, the methodological bias of this study was low.

Main analysis

Table 2 summarizes the outcomes of this meta-analysis. Minimal or no significant difference was found between the epidural steroid injection group and the epidural local anesthetic injection group for the short-term benefit, specifically, changes in the Roland–Morris Disability Questionnaire (RMDQ) Score (WMD, -1.80 , 95% CI, -2.82 to -0.78 ; $P=0.0005$) for 3 weeks, changes in the leg pain VAS score (WMD, -7.00 , 95% CI, -12.73 to -1.27 ; $P=0.02$) for 3 weeks, changes in the back pain

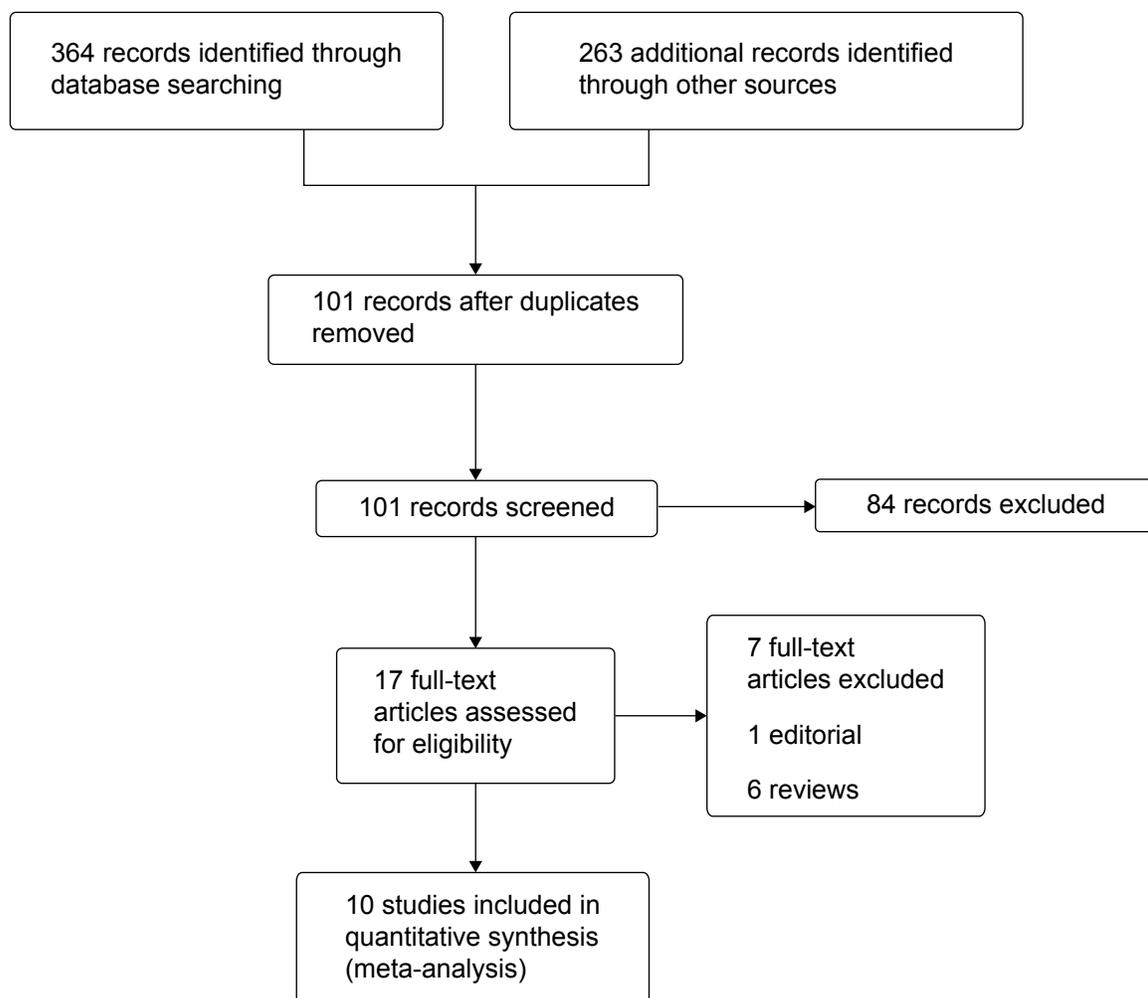


Figure 1 Flow diagram of the study identification.

Table 1 Transforaminal epidural steroid injections either with placebo or active control

Study, year	Number of patients/selection criteria	Control	Intervention	Outcome measures	Times of measurement
Cuckler et al ¹⁴ 1985	73 subjects in total, 37 with spinal stenosis, 36 with acute herniated nucleus pulposus, 37 males, 36 female, average age of 48.5 years in the experimental group and 49.5 years in the placebo group.	2 mL of saline combined with 5 mL of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb (n=31, 17 with stenosis)	2 mL of sterile water containing 80 mg of methylprednisolone acetate combined with 5 mL of 1% procaine was injected into the epidural space in the region between the 3rd and 4th lumbar vertebrae with the patient in the lateral decubitus position lying on the side of the painful limb (n=42, 20 with stenosis)	1) Subjective percentage of improvement with 75% required to be considered a treatment improvement, if less than 50% after 24 hours, was considered a treatment failure 2) Re-injection rates 3) Surgery rates	24 hours, every 3 months up to 30 months, averaging 20.2 months in the steroid group and 21.5 months in the control group
Zahaar et al ¹⁵ 1991	Experimental group average 36.6 months in symptom duration, placebo group averaged 29.4 months 30 subjects, 37 male and 26 female. Steroid group averaged 46.5 years of age and 36.6 months of symptoms. 6 months of symptoms, control group averaged 49 years of age and 29.4 months of symptoms. Setting: Medical facility in Egypt	2x2 mL of carbocaine, 4% injected into epidural space. Volume completed with sterile saline to 30 mL (n=12)	5 mL of hydrocortisone acetate suspension, 2x2 mL carbocaine, 4% volume completed with sterile saline to 30 mL (n=18)	Subjective percentage of improvement where 75% or more was deemed successful and surgery after injection was considered a failure	24 hours, then every 3 months up to 36 months averaging 20.2 months in the steroid group and 21.5 months in the control group
Fukusaki et al ¹⁶ 1998	53 subjects, 38 males and 15 female. Group 1 averaged 70 years of age and 79 days of symptoms on average, group 2 averaged 69 years of age and an average of 82 days of symptoms, group 3 averaged 72 years of age and 94 days of symptoms on average Setting: Anesthesia department in Japan	Epidural injection with 8 mL of 1% mepivacaine, repeated twice in the first week (n=18)	Epidural injection with a mixture of 8 mL of 1% mepivacaine and 40 mg of methylprednisolone, repeated twice in the first week (n=19)	Walking distance which was graded according to distance (Excellent, Good, or Poor)	1 week, 1 month, 3 months
Ng et al ¹⁷ 2005	86 patients; chronic unilateral radicular pain that failed conservative treatment	A single transforaminal epidural injection with bupivacaine only (n=43)	A single TFESI with bupivacaine and methylprednisolone (n=43). Number of injections = 1	Oswestry, VAS for back and radicular pain, change in walking distance, and patient's satisfaction level	6 and 12 weeks postinjection
Koc et al ¹⁹ 2009	29 subjects, 21 male, 8 female, average ages of 62.6, 61.1, and 53.1 years in the three groups respectively, average pain duration of 5.7 years, 5.0 years, and 5.7 years in the three groups Setting: Medical school department of physical medicine and rehabilitation in Turkey	Control group (n=10) Active controlled trial either with bupivacaine alone or bupivacaine with 40 mg of methylprednisolone	Lumbar epidural steroid injections, 10 mL of solution containing 60 mg of triamcinolon acetamide (1.5 mL), 15 mg of 0.5% bupivacaine hydrochloride (3 mL), and 5.5 mL of physiologic saline (0.9% NaCl) was injected in 3.5 minutes (n=10)	1) VAS 2) Treadmill Walk Test 3) Nottingham Health Profile 4) RMDI 5) Functional testing including finger to floor distance, sit-to-stand, and a weight carrying test VAS, ODI, LBOS	2 weeks, 1, 3, and 6 months
Tafazol et al ¹⁸ 2009	150 patients with radicular pain due to lumbar radiculitis either secondary to lumbar disc herniation or foraminal stenosis	Active controlled trial either with bupivacaine alone or bupivacaine with 40 mg of methylprednisolone. Number of injections = 1	All patients received 2 mL of 0.25% bupivacaine alone or 2 mL of 0.25% bupivacaine and 40 mg of methylprednisolone. Number of injections = 1		6 weeks, 12 weeks, 1 year

Manchikanti et al ²¹ 2012	60 patients over 30 years old with a history of chronic function-limiting low back pain and lower extremity pain of at least 6 on a scale of 0–10; pain for at least 6 months; a diagnosis of central spinal stenosis with radicular pain; patients who were competent to understand the study protocol and provide voluntary, written informed consent, and participate in outcome measurements; patients diagnosed with central spinal stenosis. And failed conservative management but not limited to, physical therapy, chiropractic manipulation, exercises, drug therapy, and bed rest	Received lumbar interlaminar injections containing a local anesthetic (lidocaine 0.5%, 6 mL)	Received lumbar interlaminar injections of 0.5% lidocaine, 5 mL, mixed with 1 mL of nonparticulate betamethasone	Mean pain relief of NRS, ODI, employment characteristics, procedure relief, opioid intake, changes in weight	3 months, 6 months, 12 months
Manchikanti et al ²⁰ 2012	100 patients with central spinal stenosis with radicular pain of at least 6 months duration and that pain must have been function-limiting, 30 years or older, and the ability to understand the study protocol and provide voluntary, written informed consent and participate in outcome measurement and failed conservative management	Epidural injections of local anesthetic (lidocaine 0.5%)	Received caudal epidural injections with 0.5% lidocaine 9 mL mixed with 1 mL of steroid, 6 mg (non-particulate betamethasone)	NRS, ODI, employment status, opioid intake, weight monitoring	3 months, 6 months, 12 months, 18 months, 24 months
Radcliff et al ²² 2013	276 patients who had neurogenic claudication or radicular leg pain with associated neurological signs, spinal stenosis as seen on cross-sectional imaging, symptoms that had persisted for at least 12 weeks	no-ESI	ESI (epidural steroid injection)	SF-36, ODI, Pain, SBI, LBPBS, LPBS	4 years
Friedly et al ²³ 2014	400 patients who had lumbar central spinal stenosis and moderate-to-severe leg pain and disability to receive epidural injections of glucocorticoids plus lidocaine or lidocaine alone	Receive epidural injections of lidocaine alone. The patients received one or two injections before the primary outcome evaluation, performed 6 weeks after randomization and the first injection	Receive epidural injections of glucocorticoids plus lidocaine. The glucocorticoid injectable solution consisted of 1 to 3 mL of 0.25% to 1% lidocaine followed by 1 to 3 mL of triamcinolone (60 to 120 mg), betamethasone (6 to 12 mg), dexamethasone (8 to 10 mg), or methylprednisolone (60 to 120 mg)	RMDQ, VAS, BPI, SSSQ, EQ-5D, PHQ-8, GAD-7	3 weeks, 6 weeks

Abbreviations: RMDQ, Roland-Morris Disability Questionnaire; VAS, visual analog scale; BPI, Brief Pain Inventory; SSSQ, Swiss Spinal Stenosis Questionnaire; SF-36, 36-Item Short Form Health Survey; EQ-5D, European Quality of Life-5 Dimensions; PHQ-8, Eight-question version of the Patient Health Questionnaire; ESI, epidural steroid injection; GAD-7, Generalized Anxiety Disorder 7 scale; LBPBS, Low Back Pain Bothersomeness Scale; ODI, Oswestry Disability Index; NRS, Numeric Rating Score; LBOs, Low back outcome score; SBI, Sciatica Bothersomeness Index; LPBS, Leg Pain Bothersomeness Index; TFES, transforaminal epidural steroid injections; RMDI, Roland Morris Disability.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cuckler et al ¹⁴ 1985	?	?	-	-	-	-	?
Friedly et al ²³ 2014	+	+	+	+	+	+	+
Fukusaki et al ¹⁶ 1998	?	?	?	-	-	-	?
Koc et al ¹⁹ 2009	?	?	+	-	-	+	?
Manchikanti et al ²⁰ 2012	+	+	?	?	+	?	?
Manchikanti L et al ²¹ 2012	?	+	+	?	+	?	+
Ng et al ¹⁷ 2005	?	+	?	?	+	+	?
Radcliff et al ²² 2013	+	+	?	+	+	+	+
Tafazal et al ¹⁸ 2009	?	+	+	?	?	+	?
Zahaar et al ¹⁵ 1991	?	?	?	-	-	-	+

Figure 2 Risk of bias summary: a review of authors' judgments about each risk of bias item for each included study.

VAS score (WMD, 0.60, 95% CI, 0.07 to 1.13; $P=0.03$) for 3 weeks, Swiss Spinal Stenosis Questionnaire (SSSQ) subscales for symptoms (WMD, -0.20, 95% CI, -0.34 to -0.06; $P=0.05$) for 3 weeks, and European Quality of Life-5 Dimensions (EQ-5D) (WMD, 0.04, 95% CI, 0.00 to 0.08; $P=0.03$) for 3 weeks. Because no significant heterogeneity was observed for the above comparisons, the fixed-effects model was subsequently used, as no significant clinical heterogeneity was found between the studies.

In terms of long-term benefit, there was significant difference between the epidural steroid injection group and the epidural local anesthetic injection group in terms of changes in bodily pain (BP) and physical function (PF) subscale scores, specifically, changes in the BP subscale scores (WMD, -11.90, 95% CI, -22.72 to -1.08; $P=0.03$) for 3 years

and (WMD, -12.90, 95% CI, -23.88 to -1.92; $P=0.02$) for 4 years and changes in the PF subscale scores (WMD, -14.30, 95% CI, -25.28 to -3.32; $P=0.01$) for 4 years. Because no significant heterogeneity was observed for the change from the BP and PF subscale scores, the fixed-effects model was subsequently used, as no significant clinical heterogeneity was found between the studies.

With respect to the epidural local anesthetic injection group, there was no significant difference for most outcome measures, such as the Brief Pain Inventory (BPI) Interference Scale (3 weeks, 6 weeks); SSSQ Physical-Function Subscales (3 weeks, 6 weeks); Eight-question version of the Patient Health Questionnaire (PHQ-8) (3 weeks, 6 weeks); Generalized Anxiety Disorder 7 (GAD-7) scale (3 weeks, 6 weeks); Oswestry Disability Index (ODI) score (6 weeks, 3 months,

Table 2 Meta-analysis of the outcomes of interest

Outcomes of interest	Times of measurement	Number of studies	Participants	Overall effect		Heterogeneity	
				Statistical method	Effect estimate	I ²	P-value
Change from RMDQ Score (0–24)	3 weeks	1	384	MD (fixed, 95% CI)	-1.80 [-2.82, -0.78]	0.0005	NA
	6 weeks	1	386	MD (fixed, 95% CI)	-1.10 [-2.21, 0.01]	0.05	NA
Change from leg pain VAS (0–100 mm)	3 weeks	1	381	MD (fixed, 95% CI)	-7.00 [-12.73, -1.27]	0.02	NA
	6 weeks	3	596	MD (fixed, 95% CI)	-3.21 [-7.86, 1.44]	0.18	0
Change from back pain VAS (0–100 mm)	3 months	2	210	MD (fixed, 95% CI)	-1.50 [-10.03, 7.03]	0.73	0
	3 weeks	1	384	MD (fixed, 95% CI)	0.60 [0.07, 1.13]	0.03	NA
	6 weeks	3	596	MD (random, 95% CI)	-1.76 [-5.06, 1.55]	0.30	84
	3 months	4	370	MD (random, 95% CI)	0.42 [-0.75, 1.59]	0.48	66
BPI Interference Scale (0–10)	6 months	2	160	MD (fixed, 95% CI)	-0.23 [-0.76, 0.31]	0.40	0
	1 year	2	160	MD (fixed, 95% CI)	-0.02 [-0.60, 0.56]	0.95	0
SSSQ subscales for symptoms (1–5)	18 months	1	100	MD (fixed, 95% CI)	0.10 [-0.65, 0.85]	0.79	NA
	2 years	1	100	MD (fixed, 95% CI)	-0.10 [-0.89, 0.69]	0.80	NA
SSSQ Physical-Function Subscales (1–4)	3 weeks	1	384	MD (fixed, 95% CI)	-0.30 [-0.86, 0.26]	0.29	NA
	6 weeks	1	386	MD (fixed, 95% CI)	-0.30 [-0.90, 0.30]	0.33	NA
EQ-5D (0–1)	3 weeks	1	384	MD (fixed, 95% CI)	-0.20 [-0.34, -0.06]	0.005	NA
	6 weeks	1	386	MD (fixed, 95% CI)	-0.10 [-0.25, 0.05]	0.19	NA
PHQ-8 (0–24)	3 weeks	1	384	MD (fixed, 95% CI)	0.00 [-0.12, 0.12]	1.00	NA
	6 weeks	1	386	MD (fixed, 95% CI)	0.10 [-0.03, 0.23]	0.13	NA
GAD-7 scale (0–21)	3 weeks	1	384	MD (fixed, 95% CI)	0.04 [0.00, 0.08]	0.03	NA
	6 weeks	1	386	MD (fixed, 95% CI)	0.02 [-0.02, 0.06]	0.31	NA
Change from BP subscale scores (0–100)	3 weeks	1	384	MD (fixed, 95% CI)	0.60 [-0.40, 1.60]	0.24	NA
	6 weeks	1	386	MD (fixed, 95% CI)	-0.40 [-1.34, 0.54]	0.40	NA
Change from PF subscale scores (0–100)	3 weeks	1	384	MD (fixed, 95% CI)	0.20 [-0.71, 1.11]	0.67	NA
	6 weeks	1	386	MD (fixed, 95% CI)	-0.30 [-1.17, 0.57]	0.50	NA
Change in ODI (0–100)	1 year	1	93	MD (fixed, 95% CI)	-5.80 [-15.32, 3.72]	0.23	NA
	2 years	1	93	MD (fixed, 95% CI)	-7.30 [-17.19, 2.59]	0.15	NA
	3 years	1	93	MD (fixed, 95% CI)	-11.90 [-22.72, -1.08]	0.03	NA
	4 years	1	93	MD (fixed, 95% CI)	-12.90 [-23.88, -1.92]	0.02	NA
	1 year	1	93	MD (fixed, 95% CI)	-7.40 [-16.92, 2.12]	0.13	NA
	2 years	1	93	MD (fixed, 95% CI)	-9.60 [-19.39, 0.19]	0.05	NA
	3 years	1	93	MD (fixed, 95% CI)	-10.60 [-21.42, 0.22]	0.05	NA
	4 years	1	93	MD (fixed, 95% CI)	-14.30 [-25.28, -3.32]	0.01	NA
	6 weeks	2	210	MD (fixed, 95% CI)	-1.56 [-6.27, 3.16]	0.52	0.29
	3 months	4	370	MD (fixed, 95% CI)	-1.76 [-3.57, 0.05]	0.06	0.94
	6 months	2	160	MD (fixed, 95% CI)	-1.61 [-3.62, 0.39]	0.11	0.81
	1 year	3	253	MD (fixed, 95% CI)	-1.69 [-3.66, 0.28]	0.09	0.44

(Continued)

Table 2 (Continued)

Outcomes of interest	Times of measurement	No of studies	Participants	Overall effect		Heterogeneity	
				Statistical method	Effect estimate	I ² %	P-value
Change from Sciatica Bothersomeness Index (0–24)	18 months	1	100	MD (fixed, 95% CI)	-0.80 [-3.38, 1.78]	NA	NA
	2 years	2	193	MD (fixed, 95% CI)	-1.72 [-4.12, 0.69]	0.22	0.22
	3 years	1	93	MD (fixed, 95% CI)	-1.10 [-9.20, 7.00]	NA	NA
	4 years	1	93	MD (fixed, 95% CI)	-6.00 [-14.32, 2.32]	NA	NA
Change from Low Back Pain Bothersomeness Scale (0–6)	1 year	1	93	MD (fixed, 95% CI)	0.90 [-1.66, 3.46]	NA	NA
	2 years	1	93	MD (fixed, 95% CI)	1.00 [-1.72, 3.72]	NA	NA
	3 years	1	93	MD (fixed, 95% CI)	-0.40 [-3.39, 2.59]	NA	NA
	4 years	1	93	MD (fixed, 95% CI)	0.50 [-2.60, 3.60]	NA	NA
Changes from weight (lbs)	1 year	1	93	MD (fixed, 95% CI)	0.00 [-0.71, 0.71]	I	NA
	2 years	1	93	MD (fixed, 95% CI)	-0.10 [-0.81, 0.61]	NA	NA
	3 years	1	93	MD (fixed, 95% CI)	-0.20 [-1.08, 0.68]	NA	NA
	4 years	1	93	MD (fixed, 95% CI)	-0.30 [-1.01, 0.41]	NA	NA
Change in Opioid Intake (Morphine Equivalence mg)	1 year	2	160	MD (fixed, 95% CI)	0.28 [-2.49, 3.04]	0.84	0.74
	2 years	1	100	MD (fixed, 95% CI)	2.00 [-1.59, 5.59]	0.27	NA
	3 months	2	160	MD (fixed, 95% CI)	-5.57 [-17.60, 6.45]	0.36	0.75
	6 months	2	160	MD (fixed, 95% CI)	-9.08 [-21.54, 3.39]	0.15	0.43
Change from LBOS	1 year	2	160	MD (fixed, 95% CI)	-9.70 [-22.19, 2.78]	0.13	0.54
	18 months	1	100	MD (fixed, 95% CI)	-6.14 [-23.46, 11.18]	0.49	NA
	2 years	1	100	MD (fixed, 95% CI)	-5.84 [-23.18, 11.50]	0.51	NA
	6 weeks	1	124	MD (fixed, 95% CI)	-1.00 [-5.85, 3.85]	0.69	NA
Further surgery	3 months	1	124	MD (fixed, 95% CI)	-0.30 [-6.27, 5.67]	0.92	NA
	1 year	1	129	RR (fixed, 95% CI)	0.65 [0.30, 1.40]	0.27	NA
Further root blocks	1 year	1	129	RR (fixed, 95% CI)	0.81 [0.34, 1.93]	0.64	NA
	6 weeks	1	86	MD (fixed, 95% CI)	-130.60 [-293.65, 32.45]	0.12	NA
Change from walking distance (yards)	3 months	1	86	MD (fixed, 95% CI)	-40.00 [-252.59, 172.59]	0.71	NA
	3 months	1	86	RR (fixed, 95% CI)	0.85 [0.59, 1.22]	0.38	NA
Discharged	3 months	1	86	RR (fixed, 95% CI)	1.14 [0.66, 1.95]	0.64	NA
	1 week	1	37	RR (fixed, 95% CI)	0.95 [0.22, 4.10]	0.94	NA
Results of treatment (Excellent and Good rate)	1 month	1	37	RR (fixed, 95% CI)	0.95 [0.06, 14.04]	0.97	NA
	3 months	1	37	RR (fixed, 95% CI)	1.42 [0.40, 5.08]	0.59	NA
Success rate > 75 percent improvement	1 day	1	37	RR (fixed, 95% CI)	1.52 [0.34, 6.81]	0.58	NA
	>20 months	1	37	RR (fixed, 95% CI)	0.30 [-22.86, 23.46]	0.98	NA
Overall average percentage of subjective improvement	1 day	1	37	MD (fixed, 95% CI)	0.30 [-22.86, 23.46]	0.98	NA
	1 day	1	37	MD (fixed, 95% CI)	0.30 [-22.86, 23.46]	0.98	NA

Note: The bold numbers mean that the effect estimate values for the contrast models are significant.

Abbreviations: CI, confidence interval; MD, Weighted Mean Difference; RR, Risk Ratio; NA, not applicable; RMDQ, Roland-Morris Disability Questionnaire; VAS, visual analog scale; BPI, Brief Pain Inventory; SSSQ, Swiss Spinal Stenosis Questionnaire; EQ-5D, European Quality of Life-5 Dimensions; PHQ-8, Eight-question version of the Patient Health Questionnaire; GAD-7, Generalized Anxiety Disorder 7 scale; ODI, Oswestry Disability Index; BP, Bodily Pain; PF, Physical Function; LBOS, Low back outcome score.

6 months, 1 year, 18 months, 2 years, 3 years, 4 years); Sciatica Bothersomeness Index (1 year, 2 years, 3 years, 4 years); Low Back Pain Bothersomeness Scale (1 year, 2 years, 3 years, 4 years); weight change (lbs) (1 year, 2 years); Opioid Intake changes (Morphine Equivalence mg) (3 months, 6 months, 1 year, 18 months, 2 years); low back outcome score (LBOS) (6 weeks, 3 months); further surgery rate (1 year); further root blocks rate (1 year); walking distance changes (yards) (6 weeks, 3 months); discharged rate (3 months); treatment results (Excellent and Good rate) (1 week, 1 month, 3 months); success rate (>75 percent improvement) (1 week, 1 month, 3 months); and overall average percentage of subjective improvement (1 day). Because no significant heterogeneity was observed for the change from the BP and PF subscale scores, the fixed-effects model was subsequently used, as no significant clinical heterogeneity was found between the studies.

Publication bias

We did not draw funnel plots because the trials for each comparison were less than ten.

Discussion

LSS is a significant problem that affects many elderly adults annually. Walking limitation due to neurogenic claudication of LSS is thought to be the hallmark of disability.²⁷ Walking ability is essential for most daily living activities and has been identified as a relatively important outcome in LSS.^{28,29} Despite the rising prevalence of LSS, only a few studies have investigated nonsurgical treatment modalities. This systematic review and meta-analysis of RCTs summarizes all of the available studies on the use of epidural steroid injection for LSS patients. We were only able to identify ten randomized, double-blind, controlled trials involving a total of 1,010 patients. Overall, the evidence described that epidural steroid injections offered minimal or no effective analgesic and do not significantly improve walking ability in LSS patients, regardless of the method of epidural injection.

Overall, epidural steroid injection treatment seems to be quite safe. While there were very few adverse effects reported in these RCTs, the safety of epidural steroid injections needs to be further evaluated. Due to the lack of significant adverse effects, epidural steroid injections are thought to be a safe treatment for future clinical research.

Now it was hard to address through meta-analysis due to the heterogeneity and diversity of the criteria in patient selection, different epidural injection approaches, doses, follow-up lengths, and differences in sample sizes. Another weakness was

the different outcome measurements, such as pain and walking ability assessments, which were measured in different ways.

In 2013, North America Spine Society's (NASS) Evidence-Based Clinical Guideline Development Committee developed an evidence-based clinical guideline³⁰ for the diagnosis and treatment of degenerative LSS. They found evidence supporting the recommendation of epidural steroid injection therapy, elaborating a B recommendation in favor of it use. However, this systematic review was based on only four^{14,16,19,31} trials.

The limitations of this meta-analysis were as follows. First, the epidural injection approaches, doses, frequencies, and duration in each trial were not exactly the same, which may have influenced the outcomes of interest. Second, some parameters of interest demonstrated a large degree of heterogeneity. The heterogeneity of change from back pain VAS score may be the result of bias from the different assessment methods used in the various trials. Last but not least, meta-analyses require greater patient numbers, and insufficient patients were included in this study. As such, larger high level studies are required to show the superiority of epidural steroid injection therapy for treating neurogenic claudication due to LSS.

Conclusion

On the basis of the reviewed trials, when compared with local anesthetic, we found no evidence that epidural steroid injection therapy provides a statistically significant improvement in pain symptoms or walking ability in LSS patients. Moreover, local anesthetic appears to play an unusual role in its efficacy for pain control. Additional better and rigorous studies with long-term observation are required to elucidate the effectiveness of epidural steroid injection treatment for LSS.

Acknowledgments

We would like to thank Run Liu for his assistance in developing the search strategy and retrieving relevant articles.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Yaksi A, Ozgonenel L, Ozgonenel B. The efficiency of gabapentin therapy in patients with lumbar spinal stenosis. *Spine (Phila Pa 1976)*. 2007;32(9):939–942.
2. Suri P, Rainville J, Kalichman L, Katz JN. Does this older adult with lower extremity pain have the clinical syndrome of lumbar spinal stenosis? *JAMA*. 2010;304(23):2628–2636.
3. Katz JN, Harris MB. Clinical practice. Lumbar spinal stenosis. *N Engl J Med*. 2008;358(8):818–825.

4. Fanuele JC, Birkmeyer NJ, Abdu WA, Tosteson TD, Weinstein JN. The impact of spinal problems on the health status of patients: Have we underestimated the effect? *Spine (Phila Pa 1976)*. 2000;25(12):1509–1514.
5. Johnsson KE, Rosen I, Uden A. The natural course of lumbar spinal stenosis. *Acta Orthop Scand Suppl*. 1993;251:67–68.
6. Winter CC, Brandes M, Muller C, et al. Walking ability during daily life in patients with osteoarthritis of the knee or the hip and lumbar spinal stenosis: A cross sectional study. *BMC Musculoskelet Disord*. 2010;11:233.
7. Iversen MD, Katz JN. Examination findings and self-reported walking capacity in patients with lumbar spinal stenosis. *Phys Ther*. 2001;81(7):1296–1306.
8. Jonsson B, Annertz M, Sjöberg C, Stromqvist B. A prospective and consecutive study of surgically treated lumbar spinal stenosis. Part I: Clinical features related to radiographic findings. *Spine (Phila Pa 1976)*. 1997;22(24):2932–2937.
9. Jansson KA, Nemeth G, Granath F, Jonsson B, Blomqvist P. Health-related quality of life (EQ-5D) before and one year after surgery for lumbar spinal stenosis. *J Bone Joint Surg Br*. 2009;91(2):210–216.
10. Taylor VM, Deyo RA, Cherkin DC, Kreuter W. Low back pain hospitalization. Recent United States trends and regional variations. *Spine (Phila Pa 1976)*. 1994;19(11):1207–1212, 1213.
11. Rajaei SS, Bae HW, Kanim LE, Delamarter RB. Spinal fusion in the United States: Analysis of trends from 1998 to 2008. *Spine (Phila Pa 1976)*. 2012;37(1):67–76.
12. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of lumbar spinal stenosis: 8 to 10 year results from the maine lumbar spine study. *Spine (Phila Pa 1976)*. 2005;30(8):936–943.
13. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study. *Spine (Phila Pa 1976)*. 2005;30(8):927–935.
14. Cuckler JM, Bernini PA, Wiesel SW, et al. The use of epidural steroids in the treatment of lumbar radicular pain. A prospective, randomized, double-blind study. *J Bone Joint Surg Am*. 1985;67(1):63–66.
15. EL ZAHAAR MS. The value of caudal epidural steroids in the treatment of lumbar neural compression syndromes. *J Neurol Orthop Med Surg*. 1991;12:181–184.
16. Fukusaki M, Kobayashi I, Hara T, Sumikawa K. Symptoms of spinal stenosis do not improve after epidural steroid injection. *Clin J Pain*. 1998;14(2):148–151.
17. Ng L, Chaudhary N, Sell P. The efficacy of corticosteroids in periradicular infiltration for chronic radicular pain: A randomized, double-blind, controlled trial. *Spine (Phila Pa 1976)*. 2005;30(8):857–862.
18. Tafazal S, Ng L, Chaudhary N, Sell P. Corticosteroids in peri-radicular infiltration for radicular pain: A randomised double blind controlled trial. One year results and subgroup analysis. *Eur Spine J*. 2009;18(8):1220–1225.
19. Koc Z, Ozcekir S, Sivrioglu K, Gurbet A, Kucukoglu S. Effectiveness of physical therapy and epidural steroid injections in lumbar spinal stenosis. *Spine (Phila Pa 1976)*. 2009;34(10):985–989.
20. Manchikanti L, Cash KA, McManus CD, Pampati V, Fellows B. Results of 2-year follow-up of a randomized, double-blind, controlled trial of fluoroscopic caudal epidural injections in central spinal stenosis. *Pain Physician*. 2012;15(5):371–384.
21. Manchikanti L, Cash KA, McManus CD, et al. Lumbar interlaminar epidural injections in central spinal stenosis: Preliminary results of a randomized, double-blind, active control trial. *Pain Physician*. 2012;15(1):51–63.
22. Radcliff K, Kepler C, Hilibrand A, et al. Epidural steroid injections are associated with less improvement in patients with lumbar spinal stenosis: A subgroup analysis of the Spine Patient Outcomes Research Trial. *Spine (Phila Pa 1976)*. 2013;38(4):279–291.
23. Friedly JL, Comstock BA, Turner JA, et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. *N Engl J Med*. 2014;371(1):11–21.
24. Parr AT, Manchikanti L, Hameed H, et al. Caudal epidural injections in the management of chronic low back pain: A systematic appraisal of the literature. *Pain Physician*. 2012;15(3):E159–E198.
25. Manchikanti L, Buenaventura RM, Manchikanti KN, et al. Effectiveness of therapeutic lumbar transforaminal epidural steroid injections in managing lumbar spinal pain. *Pain Physician*. 2012;15(3):E199–E245.
26. Moher D, Cook DJ, Jadad AR, et al. Assessing the quality of reports of randomised trials: Implications for the conduct of meta-analyses. *Health Technol Assess*. 1999;3(12):1–98.
27. Conway J, Tomkins CC, Haig AJ. Walking assessment in people with lumbar spinal stenosis: Capacity, performance, and self-report measures. *Spine J*. 2011;11(9):816–823.
28. Deen HJ, Zimmerman RS, Lyons MK, et al. Test-retest reproducibility of the exercise treadmill examination in lumbar spinal stenosis. *Mayo Clin Proc*. 2000;75(10):1002–1007.
29. Yamashita K, Hayashi J, Ohzono K, Hiroshima K. Correlation of patient satisfaction with symptom severity and walking ability after surgical treatment for degenerative lumbar spinal stenosis. *Spine (Phila Pa 1976)*. 2003;28(21):2477–2481.
30. Kreiner DS, Shaffer WO, Baisden JL, et al. An evidence-based clinical guideline for the diagnosis and treatment of degenerative lumbar spinal stenosis (update). *Spine J*. 2013;13(7):734–743.
31. Papagelopoulos PJ, Petrou HG, Triantafyllidis PG, et al. Treatment of lumbosacral radicular pain with epidural steroid injections. *Orthopedics*. 2001;24(2):145–149.

Drug Design, Development and Therapy

Publish your work in this journal

Drug Design, Development and Therapy is an international, peer-reviewed open-access journal that spans the spectrum of drug design and development through to clinical applications. Clinical outcomes, patient safety, and programs for the development and effective, safe, and sustained use of medicines are a feature of the journal, which

Submit your manuscript here: <http://www.dovepress.com/drug-design-development-and-therapy-journal>

Dovepress

has also been accepted for indexing on PubMed Central. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.