Systematic Review

A Comparative Systematic Review and Meta-Analysis of 3 Routes of Administration of Epidural Injections in Lumbar Disc Herniation

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Background: The Best Practices in Pain Management from the U.S. Department of Health and Human Services (HHS) describes interventional techniques as part of a continuum. Epidural injections are commonly utilized modalities in managing low back and lower extremity pain. Epidural injections were initially administered in 1901 where the first descriptions of caudal epidural with local anesthetic for low back pain appeared. Since then, multiple developments have occurred. Currently, epidural injections are provided by caudal, interlaminar, and transforaminal approaches. The comparative effectiveness of each modality has been studied. However, comparative assessment has been sparse.

Objectives: To assess the efficacy of 3 routes of administration of epidural injections for lumbar disc herniation.

Study Design: A systematic review and meta-analysis of randomized controlled trials (RCTs) of transforaminal, interlaminar and caudal epidural injections in managing chronic low back and lower extremity pain due to lumbar disc herniation.

Methods: RCTs with a placebo control or an active control design, performed under fluoroscopic guidance, with at least 6 months of follow-up are included. The outcome measures were pain relief and functional status improvement. Significant improvement was defined as 50% or greater pain relief and functional status improvement.

Data extraction and methodological quality assessment were performed. Evidence was summarized utilizing principles of best evidence synthesis.

Results: A total of 21 trials were included. Of these, 7 studied caudal epidural injections, whereas transforaminal epidural injections were studied in 12 trials, and lumbar interlaminar epidural injections were studied in 10 trials, which all met inclusion criteria. Based on qualitative and quantitative analysis, which included conventional dual-arm and single-arm analysis for interlaminar epidural injections, and single-arm analysis for caudal and transforaminal epidural injections, and the approach to the epidural space, there is Level I evidence for local anesthetic and steroids, Level II for local anesthetic alone for transforaminal and interlaminar approaches, and Level II for the caudal approach with steroids or local anesthetic alone for short- and long-term relief.

Limitations: There is a paucity of literature with intermediate or long-term relief of at least 6 months with appropriate outcome parameters. Conventional dual-arm meta-analysis was feasible only for interlaminar epidural injections.

Conclusion: Epidural injections with local anesthetic and steroids showed Level I evidence for transforaminal and interlaminar approaches, whereas with local anesthetic alone Level II evidence was demonstrated. In contrast, caudal epidural injections showed Level II evidence with local anesthetic with steroids or local anesthetic alone.

Key words: Chronic low back pain, lumbar radiculopathy, lumbar disc herniation, sciatica, epidural injections, local anesthetic, steroids, caudal epidural injections, interlaminar epidural injections, transforaminal epidural injections

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The clinical use of epidural injections in managing low back and lower extremity pain have been published in multiple randomized controlled trials (RCTs), systematic reviews, and evidence-based guidelines (1-13). Multiple studies have also been published with utilization patterns, expenditures, and cost utility analysis (14-19). Recent analysis of utilization patterns has revealed a decline in utilization, as well as expenditures of epidural injections in managing chronic spinal pain from 2009 to 2018 (13).

Epidural injections have been used since 1901 following the description by Sicard (20), Cathelin (21), and Pasquier and Leri (22). It is also important to note that Sicard (20,23,24) utilized local anesthetic only in caudal epidural injections and reported several weeks of improvement. Thus, during the first 50 years, treatments were limited to local anesthetic alone (6,9-11,25-27), until the reports by Robecchi and Capra (28) and Lievre et al (29) of administration of steroids through the sacral nerve root in the early 1950s were published. Epidural injections have been performed with the caudal, interlaminar or transforaminal approach. Over the years, caudal and interlaminar epidural injections have been performed more frequently than transforaminal epidural injections; however, there has been a reversing trend in recent years with a reduction in caudal and interlaminar epidural injections and increasing utilization of transforaminal epidural injections (1,14-16). Local anesthetics and corticosteroids have been commonly utilized in performing epidural injections for radiculopathy secondary to disc herniation. The rationale for neuraxial steroid use is primarily based on the benefits of neural blockades, which include pain relief that outlasts the effect based pharmacologic activity by hours, days, and sometimes weeks. Neural blockade effectiveness is based on the postulation that it alters or interrupts nociceptive input, reflex mechanisms of the afferent limb, self-sustaining activity of the neuronal pools in the neuroaxis, and the pattern of central neuronal activities (1,10,25,30,31). Thus, the focus of therapeutic activity of local anesthetics and steroids are based on the above hypothesis.

Several manuscripts as described above have evaluated the role of epidural injections and provided discordant conclusions. Further, studies have also compared various routes of administration, along with placebo control, local anesthetic alone or local anesthetic with steroids. Among the studies comparing the 3 modalities, Lee et al (7) compared the clinical efficacy between transforaminal and interlaminar epidural injections, as well as the clinical efficacy of transforaminal and caudal epidural steroid injections (8). Lee et al (7) included 27 studies to compare the benefits of transforaminal versus interlaminar epidural injections despite low-grade evidence. Due to the inconsistency and imprecision of the included studies, the authors reported more favorable, though not significant, outcomes for the transforaminal epidural for short-term of 2 weeks to one month and long-term of 4 to 6 months pain reduction, along with functional status improvement. Lee et al (8) also compared the effectiveness of transforaminal and caudal epidural injections with the inclusion of 6 studies and showed that 4 articles supported the superiority of a transforaminal epidural injection to a caudal epidural injection. Manchikanti et al (9) in a comparative systematic review and meta-analysis assessing epidural injections for lumbar radiculopathy and spinal stenosis, in response to a publication by Chou et al (12) showed similar effectiveness of the 3 approaches. Recently, Manchikanti et al (32) also assessed the available literature of fluoroscopic epidural injections performed with a minimum of 6-month follow-up showing Level I evidence for local anesthetic with steroids and Level II evidence for local anesthetic alone in disc herniation. Wei et al (33) compared transforaminal with interlaminar epidural steroid injections with the inclusion of 9 RCTs and 4 observational studies with a total of 931 patients, reaching the conclusion that transforaminal epidural steroid injection provided superior short-term pain relief.

The present systematic review with meta-analysis was undertaken to assess the efficacy or lack thereof of epidural injections with saline, local anesthetic alone, or local anesthetic with steroids, with critical evaluation and comparison of the 3 approaches.

Methods

The methodology utilized in this systematic review and meta-analysis included the utilization of the Institute of Medicine (IOM) standards for systematic reviews and comparative effectiveness research (CER) (1,32,34) and other publications relevant to systematic reviews. This systematic review is an extension of a systematic review of epidural injections with a comparative analysis of a Cochrane review (32) to further assess effectiveness with individual administration utilizing caudal, interlaminar and transforaminal approaches. There was no external funding in preparation of this manuscript and there are no undisclosed conflicts.

Date Sources and Searches

The literature search was performed through January 2021, in addition to the inclusion of all studies that were utilized in epidural guidelines (1) and a recent systematic review (32).

Study Selection

Predefined inclusion criteria included fluoroscopic guidance and reporting of at least 6 months of outcomes with RCTs with placebo – or active-controlled design. The present investigation included epidural injections with sodium chloride solution, local anesthetic, or steroids administered through caudal, interlaminar, or transforaminal approaches. Predefined outcomes were measurement of pain and function with description of composite outcomes with significant pain and functional status improvement of 50% or more.

Data Extraction and Methodologic Quality Assessment

Data extraction and quality assessment were adapted from a recent systematic review (32). Methodologic quality assessment was performed in our systematic review (32) and was adapted utilizing Cochrane review criteria (35) and Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) criteria (36).

Data Synthesis and Analysis

Data were synthesized utilizing qualitative and quantitative measurements. Evidence was assessed based on best evidence synthesis for qualitative analysis as shown in Table 1 (37).

Dual-Arm Meta-Analysis

For dual-arm meta-analysis, software Review Manager (RevMan) [Computer program] version 5.4, The Cochrane Collaboration, 2020 was used. For pain and functionality improvement data, the studies were reported as the standardized mean differences (SMD) with 95% confidence intervals (CI). Data were plotted using forest plots to evaluate treatment effects using random-effects model. Heterogeneity was interpreted through I^2 statistics.

Single-Arm Meta-Analysis

For single-arm meta-analysis, software Comprehensive Meta-Analysis version 3.0 was used (Biostat Inc., Englewood, NJ). For pain and functionality improvement data, the studies were reported as the mean differences with 95% confidence intervals. Data were plotted using forest plots to evaluate treatment effects. Heterogeneity was interpreted through I2 statistics.

Qualitative and quantitative measurements were assessed which indicated the direction of a treatment's effect and the magnitude of a treatment's effect. For placebo-controlled trials, the net effect between 2 treatments was utilized; however, for active-controlled trials, the differences between baseline and at the follow-up period were utilized (32,34).

Even though a minimum change of 20% in pain scales is widely accepted, the evolving concepts of minimal clinically important differences (MCID) have shown to be patient centered and practical. Multiple publications have alluded to the fact, adapting to the clinically relevant outcome measures defined as significant improvement with at least 50% improvement in pain and functional status (32,34). There is also ample literature documenting the necessity to use, when comparing two groups in an active control trial, changes from baseline to follow up, instead of absolute changes between groups (1,32,34).

In the present investigation, we have adapted and used either 50% relief from the baseline pain score or a change of at least 3 points on an 11-point pain scale

Table 1. ***Qualitative modified approach to grading of evidence of therapeutic effectiveness studies.***

Level I	Strong	Evidence obtained from multiple relevant high-quality randomized controlled trials
Level II	Moderate	Evidence obtained from at least one relevant high-quality randomized controlled trial or multiple relevant moderate or low-quality randomized controlled trials
Level III	Fair	Evidence obtained from at least one relevant moderate or low-quality randomized trial or Evidence obtained from at least one relevant high-quality non-randomized trial or observational study with multiple moderate or low-quality observational studies
Level IV	Limited	Evidence obtained from multiple moderate or low-quality relevant observational studies
Level V	Consensus based	Opinion or consensus of large group of clinicians and/or scientists

Modified from: Manchikanti L, et al. A modified approach to grading of evidence. *Pain Physician* 2014; 17:E319-E325 (37).

(32,34). A ≥ 30% decrease of disability scores was considered clinically significant.

Results

Figure 1 shows the literature search and selection of the manuscripts for inclusion (32). After full text review and exclusion of duplicates, we identified 21 trials (38-59) meeting inclusion criteria. Of these, a total of 7 studies assessed caudal epidural injections (38,39,48-52), 10 studies assessed interlaminar epidural injections (40-42,48,50,51,53-56), and 12 studies assessed transforaminal epidural injections (43-48,50,51,53,54,57-59).

The literature search showed a total of 21 trials met inclusion criteria (38-59). Among these, 7 studied the caudal approach, 10 studied the interlaminar approach, and 12 studied the transforaminal approach.

Among the 21 included manuscripts, one was a placebo-controlled trial (43), another trial compared epidural steroid injection with conservative management (39), 7 trials (38,40-42,44,45,47) were comparisons of local anesthetic with steroids, one trial (59) was a comparison of types of steroids, 6 trials (48,50-54) were comparisons of techniques, 3 trials (48,50,51) compared all 3 modes of administration, and 3 trials compared 2 modes of administration (52-54).

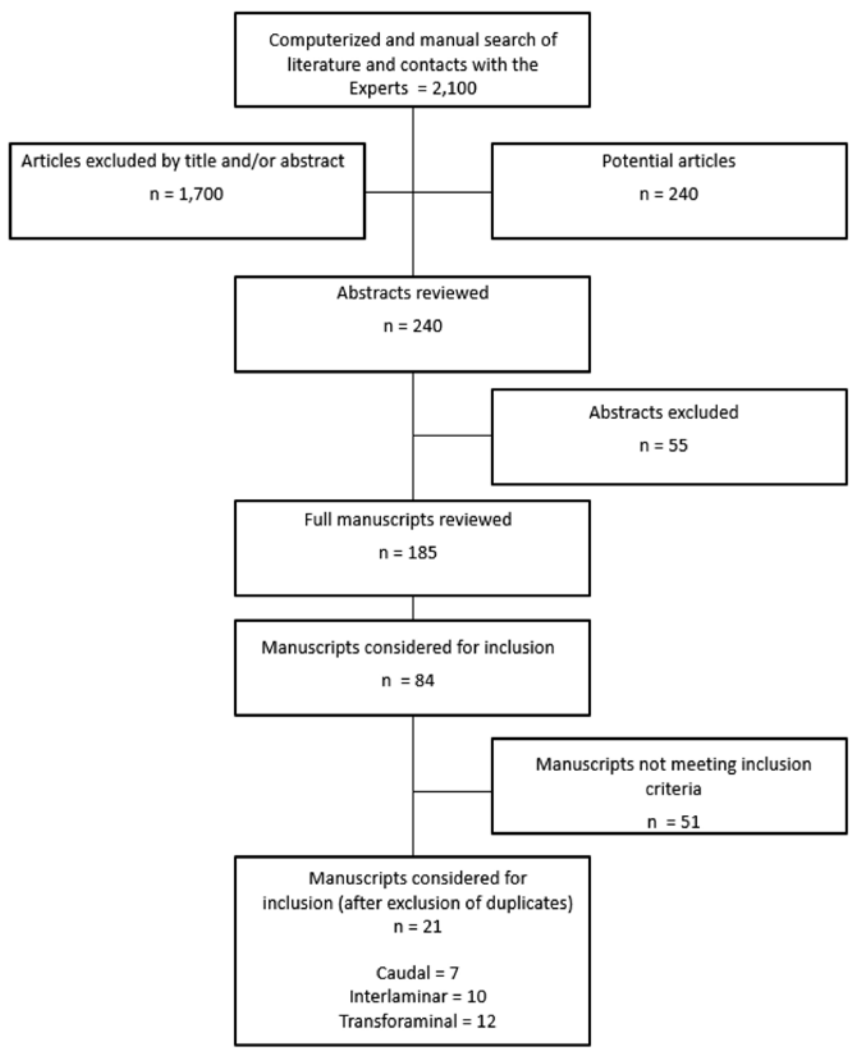


Fig. 1. *Flow diagram illustrating published literature evaluating epidural injection therapy in managing disc herniation, radiculopathy, or sciatica (32).*

Methodological Quality Assessment

Appendix Tables 1 and 2 (32) show the scoring for methodological quality assessment of all RCTs utilizing Cochrane review criteria (35) and IPM-QRB criteria (36).

This assessment shows the importance of interventional pain management-specific scoring utilizing IPM-QRB criteria, which has shown assessment results that are different from Cochrane review derived data. There was agreement between Cochrane review scoring and IPM-QRB scoring in 19 of 21 trials. The IPM-QRB scoring was shown at a lower grading than Cochrane review criteria in 2 trials (58,59).

Effectiveness of Epidural Injections

Descriptive characteristics of included studies of transforaminal, interlaminar, and caudal injections are shown in Appendix Tables 3 to 5, as adapted from our analysis (32).

Of the studies included in this assessment, there was one placebo-controlled trial (43), and one study with compared conservative management (39), 7 studies compared local anesthetic alone with local anesthetic and steroids (38,40-42,44,45,47). Appendix Table 6 shows comparison of technical aspects or dose responses.

Evidence Synthesis

Evidence synthesis was performed by qualitative and quantitative analysis.

Qualitative Synthesis

Qualitative synthesis of evidence included all 21 studies with only (38-59) one placebo-controlled trial and a second RCT compared with conservative management (39,43). All other studies were active-controlled trials. Analysis was performed for individual approaches for caudal, interlaminar, and transforaminal.

Meta-Analysis

Meta-analysis was performed utilizing conventional and single-arm analysis for transforaminal, interlaminar, and caudal approaches.

Placebo-Controlled Trials

There was only one placebo-controlled trial (43) and the second one compared epidural steroid injections with conservative management (39). Consequently, we were unable to include them in the meta-analysis with active-controlled trials.

Active-Controlled Trials

There were 19 trials utilizing active-control design. These trials underwent conventional meta-analysis, followed by single-arm meta-analysis.

Transforaminal Epidural Injections

There was only one trial meeting the inclusion criteria for conventional meta-analysis with active control and one trial with placebo control. Consequently, conventional meta-analysis was not performed. Single-arm analysis was performed as shown below.

Figure 2 shows the results of single-arm meta-analyses testing the effects of transforaminal epidural steroid injections on pain and functionality at 6 and 12 months.

In addition to the analysis of the comparative groups, we also analyzed of all the included studies irrespective of their comparative group, either related to the drugs injected or technical comparative studies if appropriate data was available. The analysis was performed for transforaminal, interlaminar, and caudal epidural injections.

Figure 2A shows the results of a single-arm meta-analysis of steroid groups from 7 studies (44,50,52-54,56,59) that were used to assess pain score after 6 months using Numeric Rating Scale (NRS) or Visual Analog Scale (VAS) in patients who underwent transforaminal epidural steroid injections. A total of 8 different points were included in the analysis because one study (59) used two different approaches. As shown in Fig. 2, the pooled mean difference of pain score from baseline to 6 months of follow-up was 4.156 points decreased (95% CI: -4.258 to – 4.054, $P < 0.001$).

Figure 2B shows the results of a single-arm meta-analysis of steroid groups from 6 studies (44,50,52-54,56) that were used to assess functionality score after 6 months using Oswestry Disability Index (ODI) or Roland-Morris Disability Questionnaire (RMDQ) in patients who underwent transforaminal epidural steroid injections. As shown in Fig. 2B, the pooled mean difference of pain score from baseline to 6 months of follow-up was 21.527 points decreased (95% CI: -22.164 to – 20.889, $P < 0.001$).

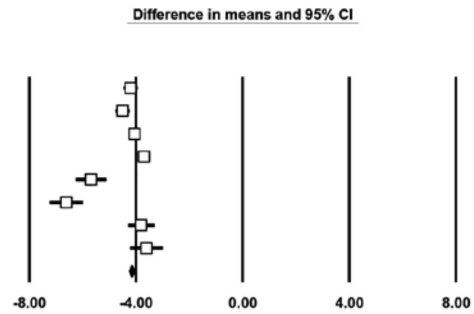
Figure 2C shows the results of a single-arm meta-analysis of steroid groups from 5 studies (44,52,54,56,57) that were used to assess pain score after 12 months using NRS or VAS in patients who underwent transforaminal epidural steroid injections. As shown in Fig. 2C, the pooled mean difference of pain score from baseline to 12 months of follow-up was 4.207 points decreased (95% CI: -4.352 to – 4.062, $P < 0.001$).

Figure 2D shows the results of a single-arm meta-analysis of steroid groups from 5 studies (44,52,54,56,57) that were used to assess the functionality score after 12 months using ODI or RMDQ in patients who underwent transforaminal epidural steroid injections. As shown in Fig. 2D, the pooled mean difference of pain score from baseline to 12 months of follow-up was 13.686 points decreased (95% CI: -14.169 to – 13.203, $P < 0.001$).

As shown in this analysis of transforaminal epidural injections, for pain relief, there were 8 studies included at 6-month follow-up, whereas only 5 studies were available for the 12-month follow-up. This analysis showed pain relief with reduction of 4.156 points with transforaminal epidural steroid injections at 6-month follow-up as shown in Fig. 2A. Further, the relief continued for 12 months with a 4.207 decrease in pain levels.

A

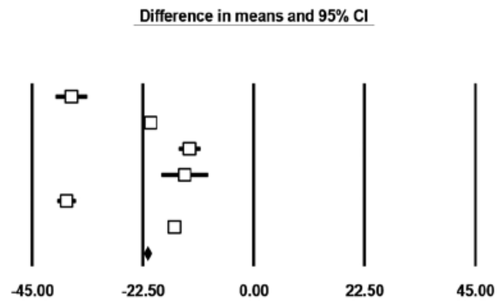
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2014 TF	-4.200	0.129	0.017	-4.453	-3.947	-32.558	0.000
Kamble et al. 2016	-4.500	0.127	0.016	-4.749	-4.251	-35.433	0.000
Singh et al. 2017	-4.050	0.102	0.010	-4.250	-3.850	-39.706	0.000
Amr 2011	-3.700	0.100	0.010	-3.896	-3.504	-37.000	0.000
Kennedy et al. 2014 D	-5.680	0.288	0.083	-6.244	-5.116	-19.722	0.000
Kennedy et al. 2014T	-6.610	0.313	0.098	-7.223	-5.997	-21.118	0.000
Ghai et al. 2014	-3.800	0.247	0.061	-4.283	-3.317	-15.416	0.000
Rados et al. 2011	-3.600	0.309	0.095	-4.206	-2.994	-11.650	0.000
	-4.156	0.052	0.003	-4.258	-4.054	-79.657	0.000



Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
124.122	7	0.000	94.360	0.400	0.283	0.080	0.632

B

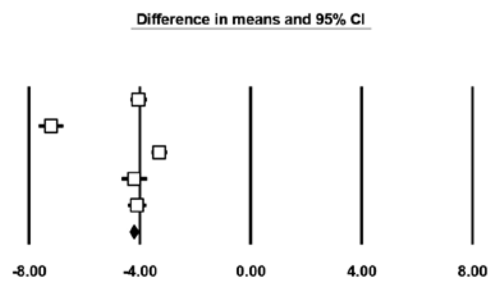
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Amr 2011	-37.000	1.600	2.560	-40.136	-33.864	-23.125	0.000
Kamble et al. 2016	-20.900	0.489	0.239	-21.859	-19.941	-42.714	0.000
Ghai et al. 2014	-13.000	1.095	1.199	-15.146	-10.854	-11.872	0.000
Rados et al. 2011	-14.000	2.386	5.693	-18.676	-9.324	-5.868	0.000
Singh et al. 2017	-38.000	0.917	0.841	-39.797	-36.203	-41.439	0.000
Manchikanti et al. 2014 TF	-16.100	0.610	0.372	-17.296	-14.904	-26.393	0.000
	-21.527	0.325	0.106	-22.164	-20.889	-66.188	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
567.613	5	0.000	99.119	85.220	71.258	5077.697	9.231

C

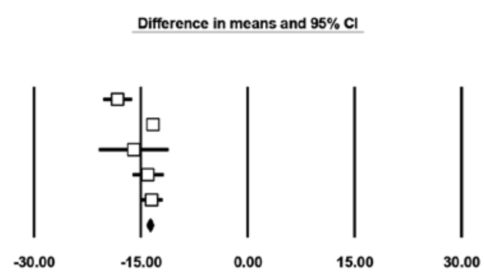
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Singh et al. 2017	-4.050	0.142	0.020	-4.328	-3.772	-28.521	0.000
Vad et al. 2002	-7.200	0.220	0.048	-7.631	-6.769	-32.727	0.000
Amr 2011	-3.300	0.135	0.018	-3.565	-3.035	-24.444	0.000
Ghai et al. 2014	-4.200	0.228	0.052	-4.647	-3.753	-18.421	0.000
Manchikanti et al. 2014 TF	-4.100	0.161	0.026	-4.416	-3.784	-25.466	0.000
	-4.207	0.074	0.005	-4.352	-4.062	-56.904	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
231.087	4	0.000	98.275	1.621	1.241	1.540	1.273

D

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Singh et al. 2017	-18.250	0.996	0.992	-20.202	-16.298	-18.323	0.000
Vad et al. 2002	-13.300	0.280	0.078	-13.849	-12.751	-47.500	0.000
Amr 2011	-16.000	2.476	6.131	-20.853	-11.147	-6.462	0.000
Ghai et al. 2014	-14.000	1.095	1.199	-16.146	-11.854	-12.785	0.000
Manchikanti et al. 2014 TF	-13.500	0.768	0.590	-15.005	-11.995	-17.578	0.000
	-13.686	0.247	0.061	-14.169	-13.203	-55.518	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
23.913	4	0.000	83.272	3.166	3.343	11.178	1.779

Fig. 2. *Results of single-arm meta-analyses testing the effects of transforaminal epidural steroid injections on pain and functionality at 6 and 12 months. A. Change in pain level at 6 months; B. Change in functionality level at 6 months; C. Change in pain level at 12 months; D. Change in functionality level at 12 months.*

Functionality also showed similar results as shown in Fig. 2B at 6 months with reduction of disability scores at 6 months of 21.527, whereas, at the 12-month follow-up (Fig. 2D), functionality score was 13.686 with significantly less improvement of disability at 12 months compared to 6-month follow-up.

Interlaminar Epidural Injections

Assessment of pain relief and functional status improvement were performed utilizing conventional dual arm analysis at 6 and 12 months (Fig. 3).

There were 3 studies (40-42) with 378 patients, which provided results eligible for dual-arm meta-analysis comparing local anesthetic and local anesthetic with steroids.

Figure 3A shows the results of a double-arm meta-analysis to assess the pain score after 6 months using NRS or VAS in patients who underwent interlaminar epidural steroid injections. As shown in Fig. 3A, the standard mean difference of pain score from baseline to 6 months of follow-up was 2.69 (0.48, 4.90), *P* = 0.002.

Figure 3B shows the results of a double-arm meta-analysis used to assess the functionality score after 6 months using ODI or RMDQ in patients who underwent interlaminar epidural steroid injections. As shown in

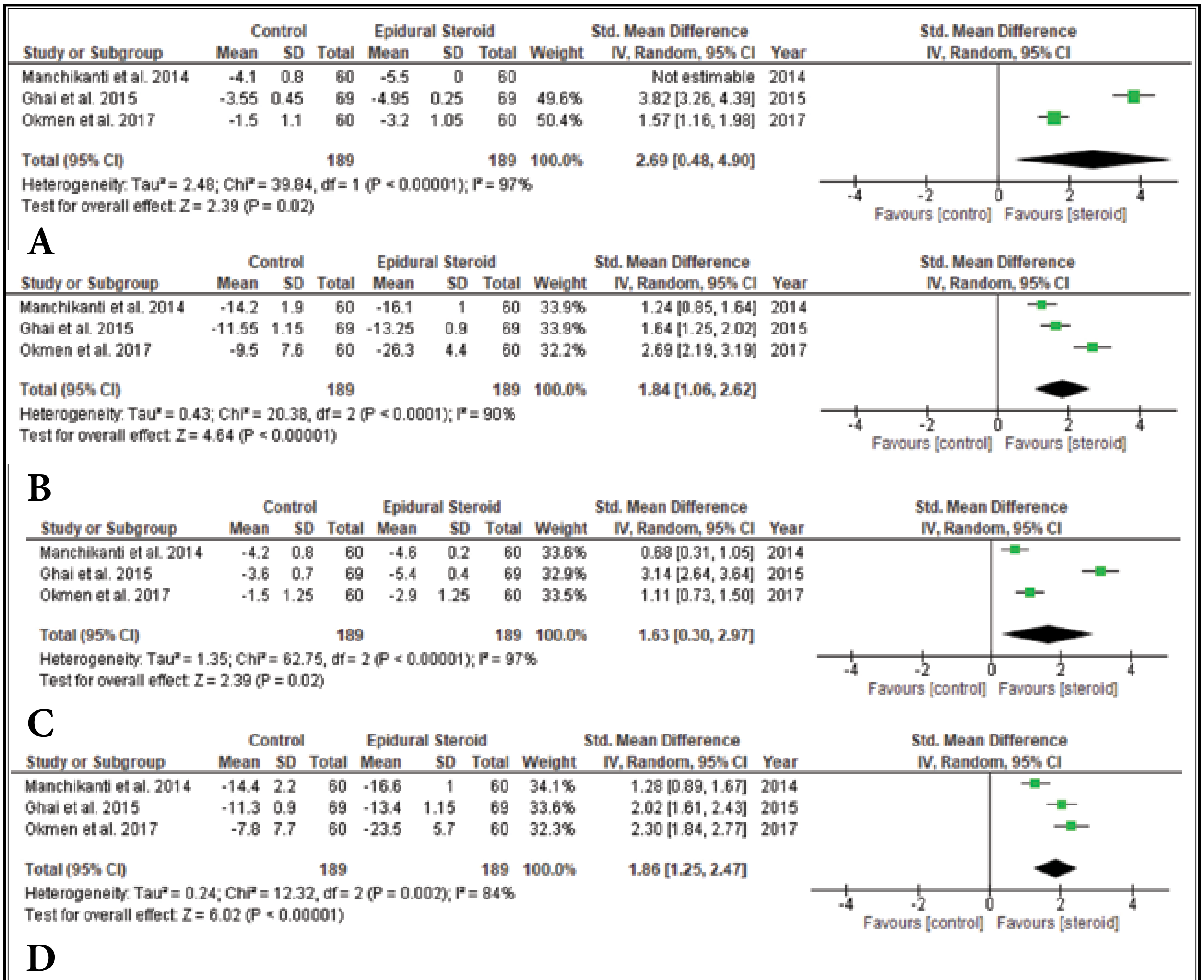


Fig. 3. *Results of dual-arm meta-analyses testing the effects of interlaminar epidural steroid injections on pain and functionality at 6 and 12 months. A. Change in pain level at 6 months; B. Change in functionality at 6 months; C. Change in pain at 12 months; D. Change in functionality at 12 months.*

Fig. 3B, the standard mean difference of functionality score from baseline to 6 months of follow-up was 1.84 (1.06, 2.62), $P < 0.001$.

Figure 3C shows the results of a double-arm meta-analysis of local anesthetic and local anesthetic with steroid groups from 3 studies (40-42) that were used to assess the pain score after 12 months using NRS or VAS in patients who underwent interlaminar epidural steroid injections. As shown in Fig. 3C, the standard mean difference of pain score from baseline to 12 months of follow-up was 1.63 (0.30, 2.97), $P = 0.02$.

Figure 3D shows the results of a dual -arm meta-analysis of local anesthetic and local anesthetic with steroid groups from 3 studies (40-42) that were used to assess the functionality score after 12 months using ODI or RMDQ in patients who underwent interlaminar epidural steroid injections. As shown in Fig. 3D, the standard mean difference of functionality score from baseline to 12 months of follow-up was 1.86 (1.25, 2.47), $P < 0.001$.

Figure 4 shows the results of single-arm meta-analysis testing the effects of interlaminar epidural steroid injections (ILESI) on pain and functionality at 6 and 12 months.

Figure 4A shows the results of a single-arm meta-analysis of steroid groups from 7 studies (40-42,50,53-55) that were used to assess the pain score after 6 months using NRS or VAS in patients who underwent interlaminar epidural steroid injections. A total of 8 different points were included in the analysis because one study (55) used 2 different approaches. As shown in Fig. 4A, the pooled mean difference of pain score from baseline to 6 months of follow-up was 4.186 points decreased (95% CI: -4.323 to – 4.050, $P < 0.001$).

Figure 4B shows the results of a single-arm meta-analysis testing the effects of ILESI on functionality at 6 months. Figure 4B shows the results from control groups of 7 studies (40-42,50,53-55) assessing functionality scores after 6 months using ODI or RMDQ. As shown in Fig. 4B, the pooled mean difference of pain score from baseline to 6 months of follow-up was 14.500 points decreased (95% CI: -14.653 to – 14.347, $P < 0.001$).

Figure 4C shows the results of a single-arm meta-analysis of steroid groups from 5 studies (40-42,54,55) that were used to assess pain score after 12 months using NRS or VAS in patients who underwent interlaminar epidural steroid injections. A total of 6 different points were included in the analysis because one study (55) used two different approaches. As shown in Fig. 4C, the pooled mean difference of pain score from baseline to 12 months of follow-up was 4.545 points decreased (95% CI: -4.595 to – 4.495, $P < 0.001$).

Figure 4D shows the results of a single-arm meta-analysis of steroid groups from 5 studies (40-42,54,55) that were used to assess the functionality score after 12 months using ODI or RMDQ in patients who underwent interlaminar epidural steroid injections. A total of 6 different points were included in the analysis because one study (55) used two different approaches. As shown in Fig. 4D, the pooled mean difference of pain score from baseline to 12 months of follow-up was 15.227 points decreased (95% CI: -15.408 to – 15.045, $P < 0.001$).

Single-arm analysis with pain and functionality at 6 and 12 months showed significant effectiveness of lumbar interlaminar epidural injections with steroids as shown in Fig. 4A. At the 6-month follow-up, there was a decrease in pain scores of 4.186 points with a 4.545-point decrease at the 12-month follow-up. Functionality also showed significant improvement with disability as shown in Fig. 4B. There was a significant decrease in disability with 14.500 points at 6-month follow-up with a 15.227-point decrease (Fig. 4D) at 12-month follow-up.

Caudal Epidural Injections

Conventional dual arm analysis was not performed at 6 and 12 months for caudal epidural injections for pain relief and functional status improvement due to lack of eligible studies.

Figure 5 shows the results of a single-arm meta-analysis testing the effects of caudal epidural steroid injections (CESI) on pain and functionality at 6 and 12 months.

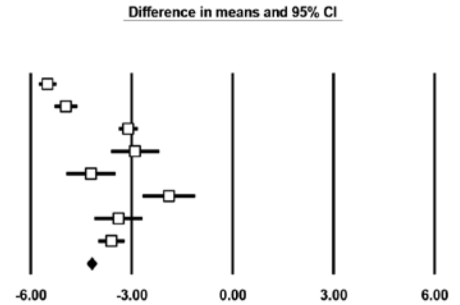
Figure 5A shows the results of a single-arm meta-analysis of steroid groups from 3 studies (38,50,52) that were used to assess pain score after 6 months using NRS or VAS in patients who underwent caudal epidural steroid injections. As shown in Fig. 5A, the pooled mean difference of the pain score from baseline to 6 months of follow-up was 3.836 points decreased (95% CI: -3.899 to – 3.774, $P < 0.001$).

Figure 5B shows the results of a single-arm meta-analysis of steroid groups from 3 studies (38,50,52) that were used to assess functionality score after 6 months using ODI or RMDQ in patients who underwent caudal epidural steroid injections. As shown in Fig. 5B, the pooled mean difference of pain score from baseline to 6 months of follow-up was 16.361 points decreased (95% CI: -16.462 to – 16.261, $P < 0.001$).

Figure 5C shows the results of a single-arm meta-analysis of steroid groups from 2 studies (38,52) that were used to assess pain score after 12 months using NRS or VAS in patients who underwent caudal epidural

A

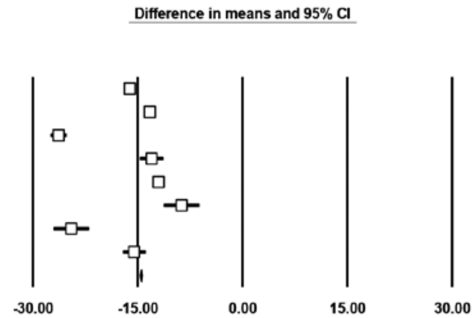
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2014 IL	-5.500	0.129	0.017	-5.753	-5.247	-42.636	0.000
Ghai et al. 2015	-4.950	0.170	0.029	-5.283	-4.617	-29.118	0.000
Okmen & Okmen 2017	-3.100	0.136	0.018	-3.367	-2.833	-22.794	0.000
Rados et al. 2011	-2.900	0.362	0.131	-3.610	-2.190	-8.011	0.000
Ghai et al. 2014	-4.210	0.371	0.138	-4.937	-3.483	-11.348	0.000
Candido et al. 2013 MIL	-1.890	0.392	0.154	-2.658	-1.122	-4.821	0.000
Candido et al. 2013 PIL	-3.390	0.361	0.130	-4.098	-2.682	-9.391	0.000
Kamble et al. 2016	-3.600	0.192	0.037	-3.976	-3.224	-18.750	0.000
	-4.186	0.070	0.005	-4.323	-4.050	-59.936	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
248.825	7	0.000	97.187	1.487	1.036	1.074	1.219

B

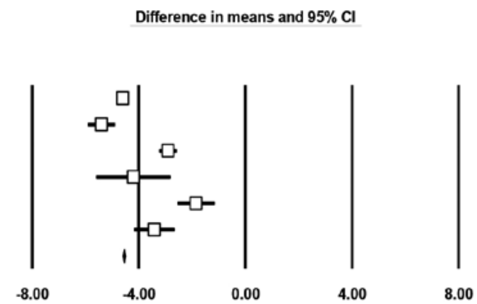
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2014 IL	-16.100	0.129	0.017	-16.353	-15.847	-124.806	0.000
Ghai et al. 2015	-13.250	0.108	0.012	-13.462	-13.038	-122.685	0.000
Okmen & Okmen 2017	-26.300	0.568	0.323	-27.413	-25.187	-46.303	0.000
Ghai et al. 2014	-13.000	0.840	0.705	-14.646	-11.354	-15.484	0.000
Rados et al. 2011	-12.000	0.301	0.091	-12.590	-11.410	-39.867	0.000
Candido et al. 2013 MIL	-8.700	1.279	1.636	-11.207	-6.193	-6.802	0.000
Candido et al. 2013 PIL	-24.500	1.266	1.603	-26.981	-22.019	-19.352	0.000
Kamble et al. 2016	-15.500	0.812	0.659	-17.091	-13.909	-19.089	0.000
	-14.500	0.078	0.006	-14.653	-14.347	-185.770	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
876.031	7	0.000	99.201	9.004	9.651	93.138	3.001

C

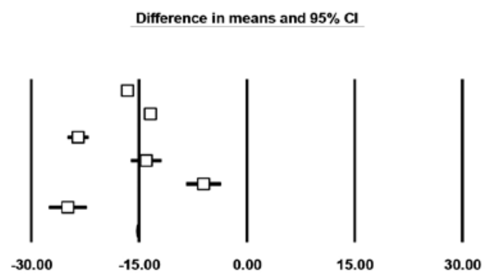
Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2014 IL	-4.600	0.026	0.001	-4.651	-4.549	-176.923	0.000
Ghai et al. 2015	-5.400	0.259	0.067	-5.908	-4.892	-20.849	0.000
Okmen & Okmen 2017	-2.900	0.161	0.026	-3.216	-2.584	-18.012	0.000
Ghai et al. 2014	-4.200	0.707	0.500	-5.586	-2.814	-5.941	0.000
Candido et al. 2013 MIL	-1.850	0.350	0.123	-2.536	-1.164	-5.286	0.000
Candido et al. 2013 PIL	-3.410	0.385	0.148	-4.165	-2.655	-8.857	0.000
	-4.545	0.025	0.001	-4.595	-4.495	-178.926	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
187.987	5	0.000	97.340	1.341	1.377	1.895	1.158

D

Study name	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Manchikanti et al. 2014 IL	-16.600	0.129	0.017	-16.853	-16.347	-128.682	0.000
Ghai et al. 2015	-13.400	0.138	0.019	-13.670	-13.130	-97.101	0.000
Okmen & Okmen 2017	-23.500	0.736	0.542	-24.943	-22.057	-31.929	0.000
Ghai et al. 2014	-14.000	1.060	1.124	-16.078	-11.922	-13.208	0.000
Candido et al. 2013 MIL	-6.040	1.220	1.488	-8.431	-3.649	-4.951	0.000
Candido et al. 2013 PIL	-24.920	1.340	1.796	-27.546	-22.294	-18.597	0.000
	-15.227	0.093	0.009	-15.408	-15.045	-164.398	0.000



Heterogeneity				Tau-squared			
Q-value	df (Q)	P-value	I-squared	Tau Squared	Standard Error	Variance	Tau
525.276	5	0.000	99.048	8.406	10.815	116.960	2.899

Fig. 4. *Results of single-arm meta-analysis testing the effects of interlaminar epidural steroid injections (ILESI) on pain and functionality at 6 and 12 months. A. Change in pain level at 6 months; B. Change in functionality level at 6 months; C. Change in pain level at 12 months; D. Change in functionality level at 12 months.*

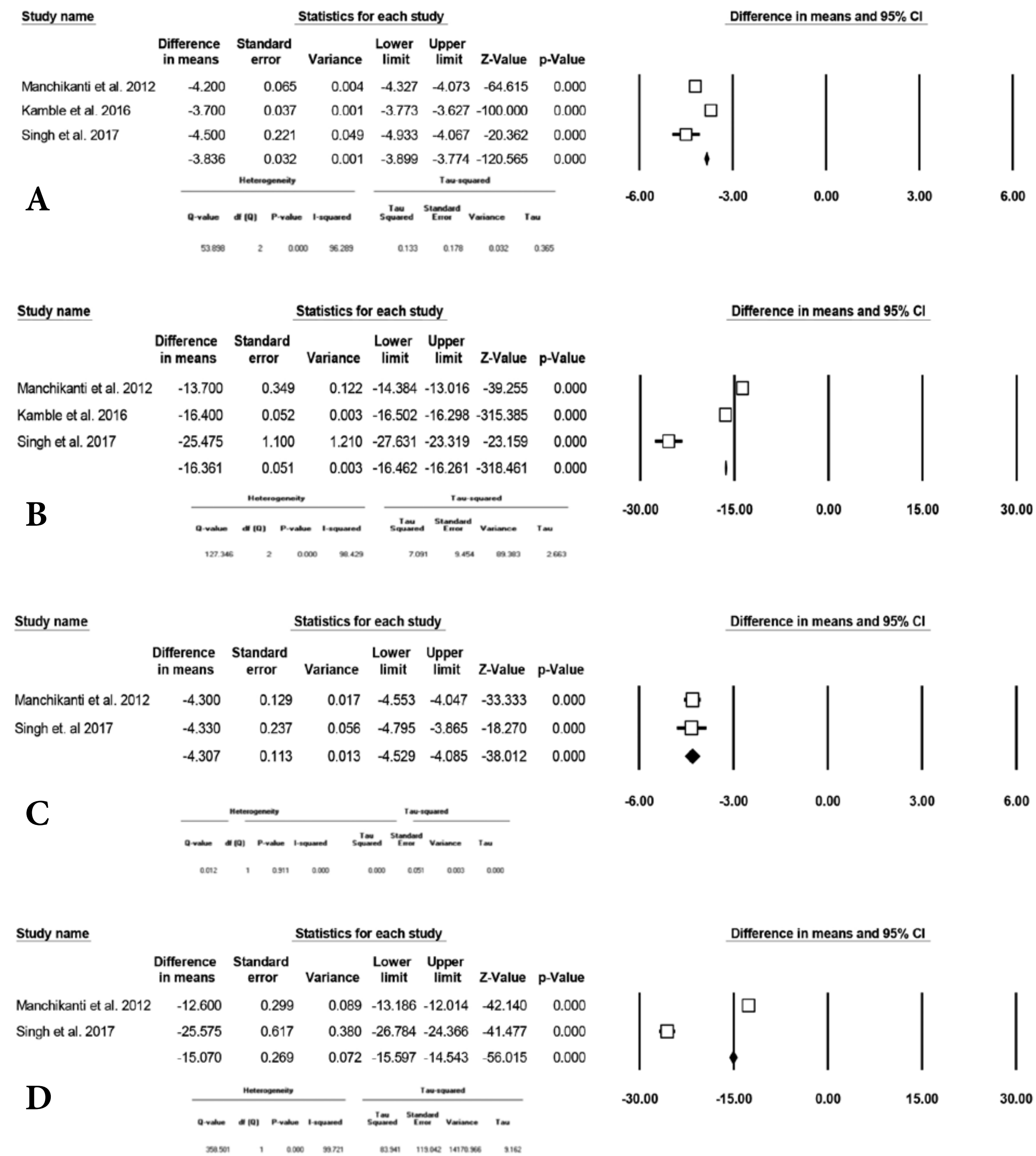


Fig. 5. *Results of single-arm meta-analysis testing the effects of caudal epidural steroid injections (CESI) on pain and functionality at 6 and 12 months. A. Change in pain level at 6 months; B. Change in functionality level at 6 months; C. Change in pain level at 12 months; D. Change in functionality level at 12 months.*

steroid injections. As shown in Fig. 5C, the pooled mean difference of pain score from baseline to 12 months of follow-up was 4.307 points decreased (95% CI: -4.529 to – 4.085, $P < 0.001$).

Figure 5D shows the results of a single-arm meta-analysis of steroid groups from 2 studies (38,52) that were used to assess functionality score after 12 months using ODI or RMDQ in patients who underwent caudal epidural steroid injections. As shown in Fig. 5D, the pooled mean difference of pain score from baseline to 12 months of follow-up was 15.070 points decreased (95% CI: -15.597 to – 14.543, $P < 0.001$).

Similar to transforaminal and interlaminar epidural injections in the lumbar spine, caudal epidural injections also showed a significant improvement with single-arm analysis at 6 months and 12 months with pain relief and functional status improvement. As shown in Fig. 5A, there was decrease of pain ratings of 3.836 at 6 months and 4.307 points at 12-month follow-up. Functionality also showed similar results with a decrease of disability of 16.361 points at 6 months and 15.070 points at 12 months.

Analysis of Evidence

Based on the qualitative synthesis of evidence of 21 RCTs with one negative or inconclusive trial, the evidence is Level I for short and long-term improvement for epidural injections with local anesthetic with steroids and Level II with local anesthetic alone.

Based on the qualitative analysis with positive results of 10 of 11 trials, the evidence is considered as strong at Level I for transforaminal epidural injections with local anesthetic and steroids, whereas it is Level II for local anesthetic alone.

Based on the qualitative analysis of evidence for evidence for interlaminar epidural injections is Level I with local anesthetic and steroids and Level II with local anesthetic alone.

Based on the qualitative analysis, the evidence is Level II for caudal epidural injections with local anesthetic with steroids or with local anesthetic alone for short- and long-term improvement.

Discussion

The present systematic review and meta-analysis comparing transforaminal, interlaminar, and caudal approaches with qualitative and quantitative analysis showed Level I evidence for caudal, interlaminar, and transforaminal epidural injections in managing lumbar disc herniation with local anesthetic with steroids or local anesthetic alone. Based on the qualitative and quantitative analysis, which included conventional dual-arm and single-arm meta-analysis and approach to the epidural space, there is Level I evidence with local anesthetic and steroids, whereas the evidence is Level II for local anesthetic alone for transforaminal, and interlaminar approaches, and Level II for the caudal approach with steroids or local anesthetic alone for short-term and long-term relief.

Among 21 RCTs, 7 studied the role of caudal epidural injections, whereas interlaminar epidural injections were studied in 10 studies, and transforaminal epidural injections in 12 studies. For qualitative analysis, all 21 studies were included. The conventional dual-arm analysis showed no significant difference with local anesthetics alone compared to local anesthetics and steroids with pain and functionality. There was an initial trend of superiority with pain relief at 6 and 12 months; however, the trend was more evident with functionality both at 6 and 12 months. Further, single-arm analysis expanded inclusion of the studies with 6 to 8 studies for transforaminal epidural studies alone showing significant improvement from baseline with pain and functionality. For interlaminar steroids, a total of 7 studies were included, which showed results of significant improvement with pain and function at 6 and 12 months. Caudal epidural steroids only had 3 studies eligible at 6-month follow-up and only 2 studies at 12-month follow-up. Nevertheless, the results showed significant efficacy of epidural steroids by all approaches.

Based on the qualitative synthesis of evidence of one placebo-controlled trial (43), transforaminal epidural steroid injections with bupivacaine, with saline showed a lack of effectiveness. Karpinnen et al (43) performed this trial in 2001 with an injection of methylprednisolone and bupivacaine in 80 patients and sodium chloride solution in 80 patients. At 3 months they showed significant treatment effect in favor of the saline solution for back pain, and at 6 months for back pain and leg pain. At 12 months, there were no treatment effects in favor of either treatment. Even though this is considered to be a negative study, the authors performed a subgroup analysis and adjusted between group treatment differences at each follow-up assessment with number of patients free of leg pain utilizing a cut-off of 75% improvement, and efficacy by the area-under-the-curve method (60). For the cost effectiveness estimate, the total costs were divided by the number of responders. The results showed that in the cases of contained herniations, the steroid injection produced significant treatment effects and short-term efficacy in leg pain. However, for symptomatic lesions at L3-L4-L5, steroid was superior to saline for leg pain, disability, and straight leg raising in the short term. By one-year, steroids seemed to have prevented operations for contained herniations, costing $12,666 less per responder in the steroid group. For extrusions, steroids seemed to increase the operation rate, and the steroid infiltration was more expensive, costing $4,445 per responder. However, this was an inappropriate placebo design without applicable results in the primary study. Essentially, the authors recanted the results of the primary study. Consequently, this may be considered as a positive study.

The second RCT (39) compared caudal epidural with local anesthetic and methylprednisolone with conservative management. Murakibhavi and Khemka (39) in 2011 assessed 50 patients with controlled conservative management and an additional 52 patients with caudal epidural with lidocaine and methylprednisolone. At the 6-month follow-up, they showed 24% improvement in the conservative management group compared to 80% in the treatment group with epidural injections.

The remaining 19 studies with various characteristic features of comparison with local anesthetic and steroids, comparison of non-particulate and particulate steroids, comparison of technique with caudal, interlaminar, and transforaminal approaches, comparison of preganglionic and postganglionic approaches, comparison of trigger point injections with epidural steroids, and, finally, comparison of caudal epidural injection with endoscopic decompression in non-surgical patients. All of them showed positive results on a short-term and long-term basis. For transforaminal epidural injections, there were 12 trials. Of these, Karppinen et al (43,60) were controversial. Among the other 11 trials, 6 trials (44,45,47,51,54,57) showed long-term analysis of the results with long-term follow-up with positive results at one-year follow-up. The remaining trials were of short-term duration; however, they also showed positive short-term results. Of these, 2 trials (44,47) compared lidocaine with steroids and one study bupivacaine alone or bupivacaine with steroids was compared (45). Overall, results were similar in both groups with lidocaine alone compared to lidocaine with steroids; however, bupivacaine with steroids showed significantly superior effect with bupivacaine with steroids and also avoided surgery in 71% of the steroid group compared to 33% of bupivacaine group.

For caudal epidural injections, there were a total of 7 trials included in this analysis. There was one controlled trial comparing conservative management to local anesthetic and steroid treatment (39), showing 80% positive rate in the steroid group with 24% in the conservative management group. In contrast, only one study evaluated the role of caudal epidural injections (38) with comparative analysis of lidocaine alone or lidocaine with steroids and showed at the end of the one-year 67% positive improvement with local anesthetic and 72% improvement with the steroid group. However, when they considered only responsive patients, the improvement was seen in 85% of the patients with local anesthetic compared to 84% with local anesthetic and steroids. Overall, both groups showed similar results even though the superiority of steroids was shown elicited with average pain relief for steroids. Other studies compared caudal, interlaminar, versus transforaminal or caudal with transforaminal with improvement seen in all groups. Further, in one study (49), response to caudal epidural with local anesthetic and steroid was assessed with endoscopy showing significant improvement in both groups. Thus, results in qualitative analysis show that one active control trial comparing local anesthetic alone with local anesthetic and steroids (38) and one active control trial comparing 3 techniques with one-year follow-up showed positive results. The remaining studies were of short-term follow-up.

For interlaminar epidural injections, there were 10 trials with all showing positive results (40-42,48,50-56). There were 7 trials showing long-term improvement (40-42,51,54-56). There was significant evidence of effectiveness of local anesthetic alone; however, with local anesthetic with steroids, either lidocaine or bupivacaine was shown to be superior to local anesthetic alone.

Our results are in concordance with guidelines and multiple other systematic reviews (1-9). A systematic review by Manchikanti et al (3) evaluated if epidural injection of sodium chloride solution was true placebo or it is an active control agent with performance of conventional dual-arm and a single-arm analysis. The analysis with inclusion of 8 trials meeting inclusion criteria, with only 2 trials utilizing fluoroscopic imaging, and one study utilizing ultrasound, showed no significant difference between epidural sodium chloride solution and epidural steroids with sodium chloride solution with dual-arm analysis. However, when they applied single arm analyses, both epidural saline and epidural steroids with saline were effective in reducing 20% of pain; however, only reducing disability scores by 10% to 12%. The authors concluded that both epidural saline and epidural steroids with saline showed effects beyond placebo with strong evidence that neither epidural saline, nor epidural steroids with saline or placebo and that both are effective.

In another systematic review and meta-analysis, Manchikanti et al (4) assessed the effectiveness of epidural bupivacaine with or without steroids administered for low back and lower extremity pain with inclusion of 4 studies. In this review, both conventional dual-arm and single-arm meta-analysis showed significant effectiveness of both bupivacaine and bupivacaine with steroids. This review concluded that epidurally administered bupivacaine acts as an active agent rather than a placebo with Level I evidence, and that bupivacaine administered alone was almost equally effective as when administered with steroids (Level II evidence). These findings clearly showed that bupivacaine is not a placebo and the approach in all the active-controlled trials with local anesthetic converting into placebo-controlled trials and subsequently concluding that local anesthetics are ineffective leads to inappropriate conclusions and misinformation.

Knezevic et al (5), in a systematic review and meta-analysis including dual-arm and single-arm analysis, investigated the role of epidural lidocaine, with or without steroids, in managing spinal pain. In this analysis, 15 manuscripts were included with 4 addressing caudal epidural injections, 2 lumbar transforaminal injections, and 5 lumbar interlaminar epidural injections. The results showed similar improvements in pain and function with epidural administration of lidocaine alone or with steroids, both for short- and long-term, Level II evidence. This study also once again demonstrated that utilizing single-arm analysis, the clear effect on each modality was demonstrated with lidocaine, as well as lidocaine with steroids. Consequently, once again, it was shown that it is inappropriate to judge that lidocaine is a placebo.

Similar to the above manuscripts, Lee et al (6), with the inclusion of 14 manuscripts, showed that the addition of steroids to local anesthetics or saline provided better effectiveness compared to injection of local anesthetics or saline without steroids. Mesregah et al (61) also evaluated cervical interlaminar epidural injections with or without local anesthetic with the conclusion that the addition of steroids to lidocaine was not associated with better pain and functional score outcomes compared with anesthetic injected alone. Zhao et al (2), also in a systematic review and meta-analysis, confirmed that in the management of lumbar disc herniation and lumbar spinal stenosis, the effects were similar with lidocaine with or without the addition of steroids.

Discordant conclusions (17-19) brought on multiple challenges related to the conduct of the RCTs based on approach (transforaminal, interlaminar, or caudal), control design (active-control versus placebo-control), technical performance (with or without fluoroscopy), alternate techniques, and outcomes assessments (absolute difference between 2 groups or MCID with assessment of proportion of patients). The IOM (34,62) described multiple issues related to the design of the systematic reviews related to inclusion criteria (placebo versus active-control or all active controls converted to placebo), methodological quality assessment of the trials, outcomes assessment, and perceived intellectual bias with conflicts of interest. IOM also extensively described the role of bias and conflicts of interest and the need to minimize the bias and conflicts of interest. IOM defined conflict of interest as, "a set of circumstances that creates a risk that professional judgement or actions regarding the primary interest will be unduly influenced by a secondary interest." While primary interests are well known with financial conflicts of interest, IOM has described secondary interests, such as the pursuit of professional advancement, future funding opportunities and recognition, and the desire to do favors for friends and colleagues, as potential conflicts. In fact, such descriptions have been provided in the past illustrating hidden conflicts of interest not only by academicians, but by agencies which advise the policy makers and those preparing reviews for these organizations (1,3-5,9-13,30,32,34,62-67). Additionally, along the same lines, the Institute for Transitional Medicine and Therapeutics has described confluence (not conflict of interest) in which they describe conflicts of interest represents a complex ecosystem that requires development of a uniform approach to minimize bias in clinical research across the academic sector (63). They showed that the term conflict of interest is pejorative, disclosure policies have focused on financial gains only, whereas in academia the prospect of fame may be even more seductive than fortune. We believe that multiple reviews suffer from intellectual bias and undisclosed confluence of interest, tainting the value of the publications.

Conclusion

Epidural injections with local anesthetic and steroids showed Level I evidence for transforaminal and interlaminar approaches, whereas with local anesthetic alone Level II evidence was shown. In contrast, caudal epidural injections showed Level II evidence with local anesthetic with steroids or local anesthetic alone.

Author Contributions

The study was designed by LM, NK, AA, ADK and JK. Statistical analysis was performed by EK and NK. All authors contributed to preparation to the manuscript, reviewed, and approved the content with final version.

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Supplemental material available at www.painphysicianjournal.com

References

1. Manchikanti L, Knezevic NN, Navani A, et al. Epidural interventions in the management of chronic spinal pain: American Society of Interventional Pain Physicians (ASIPP) comprehensive evidence-based guidelines. *Pain Physician* 2021; 24:S27-S208.
2. Zhao W, Wang Y, Wu J, et al. Long-term outcomes of epidurals with lidocaine with or without steroids for lumbar disc herniation and spinal stenosis: A meta-analysis. *Pain Physician* 2020; 23:365-374.
3. Manchikanti L, Knezevic NN, Sanapati J, et al. Is epidural injection of sodium chloride solution a true placebo or an active control agent? A systematic review and meta-analysis. *Pain Physician* 2021; 24:41-59.
4. Manchikanti L, Knezevic NN, Parr A, Kaye AD, Sanapati M, Hirsch JA. Does epidural bupivacaine with or without steroids provide long-term relief? A systematic review and meta-analysis. *Curr Pain Headache Rep* 2020; 24:26.
5. Knezevic N, Manchikanti L, Urits I, et al. Lack of superiority of epidural injections with lidocaine with steroids compared to without steroids in spinal pain: A systematic review and meta-analysis. *Pain Physician* 2020; 23:S239-S270.
6. Lee JH, Kim DH, Kim DH, et al. Comparison of clinical efficacy of epidural injection with or without steroid in lumbosacral disc herniation: A systematic review and meta-analysis. *Pain Physician* 2018; 21:449-468.
7. Lee JH, Shin KS, Park SJ, et al. Comparison of clinical efficacy between transforaminal and interlaminar epidural injections in lumbosacral disc herniation: A systematic review and meta-analysis. *Pain Physician* 2018; 21:433-448.
8. Lee JH, Shin KH, Bahk SJ, et al. Comparison of clinical efficacy of transforaminal and caudal epidural steroid injection in lumbar and lumbosacral disc herniation: A systematic review and meta-analysis. *Spine J* 2018; 18:2343-2353.
9. Manchikanti L, Knezevic NN, Boswell MV, Kaye AD, Hirsch JA. Epidural injections for lumbar radiculopathy and spinal stenosis: A comparative systematic review and meta-analysis. *Pain Physician* 2016; 19:E365-E410.
10. Bogduk N, Christophidis N, Cherry D, et al. Epidural use of steroids in the management of back pain. Report of working party on epidural use of steroids in the management of back pain. National Health and Medical Research Council Commonwealth of Australia, Canberra 1994, pp 1-76.
11. Pinto RZ, Maher CG, Ferreira ML, et al. Epidural corticosteroid injections in the management of sciatica: A systematic review and meta-analysis. *Ann Intern Med* 2012; 157:865-877.
12. Chou R, Hashimoto R, Friedly JL, et al. Epidural corticosteroid injections for radiculopathy and spinal stenosis: A systematic review and meta-analysis. *Ann Intern Med* 2015; 163:373-381.
13. Oliveira CB, Maher CG, Ferreira ML, et al. Epidural corticosteroid injections for lumbosacral radicular pain. *Cochrane Database Syst Rev* 2020; 4:CD013577.
14. Manchikanti L, Sanapati MR, Pampati V, Boswell MV, Kaye AD, Hirsch JA. Update on reversal and decline of growth of utilization of interventional techniques in managing chronic pain in the Medicare population from 2000 to 2018. *Pain Physician* 2019; 22:521-536.
15. Manchikanti L, Sanapati MR, Soin A, et al. An updated analysis of utilization of epidural procedures in managing chronic pain in the Medicare population from 2000 to 2018. *Pain Physician* 2020; 23:111-126.
16. Manchikanti L, Pampati V, Soin A, Sanapati MR, Kaye AD, Hirsch JA. Declining utilization and inflation-adjusted expenditures for epidural procedures in chronic spinal pain in the Medicare population. *Pain Physician* 2021; 24:1-15.
17. Manchikanti L, Kaye AD, Soin A, et al. Comprehensive evidence-based guidelines for facet joint interventions in the management of chronic spinal pain: American Society of Interventional Pain Physicians (ASIPP) guidelines. *Pain Physician* 2020; 23:S1-S127.
18. Manchikanti L, Manchikanti MV, Vanaparthy R, Kosanovic R, Pampati V. Utilization patterns of sacroiliac joint injections from 2000 to 2018 in fee-for-service Medicare population. *Pain Physician* 2020; 23:439-450.
19. Manchikanti L, Pampati V, Soin A, et al. Trends of expenditures and utilization of facet joint interventions in fee-for-service (FFS) Medicare population from 2009-2018. *Pain Physician* 2020; 23:S129-S147.

20. Sicard MA. Les injections medicamenteuse extradurales par voie saracoccygiene. C R Seances Soc Biol Fil 1901; 53:396-398.
21. Cathelin F: Une nouvelle voie d'injection rachidienne: méthode des injections épidurales par le procédé du canal sacre - applications à l'homme. *Compt Rend Soc de Biol* 1901; 53:452-453.
22. Pasquier MM, Leri D. Injection intra-et extradurales de cocaine a dose minime daus le traitments dela sciatique. *Bull Gen Ther* 1901; 142:196.
23. Ter Meulen BC, Weinstein H, Ostelo R, Koehler PJ. The epidural treatment of sciatica: Its origin and evolution. *Eur Neurol* 2016; 75:58-64.
24. Steimlé R. Jean A. Sicard (1872-1929). *J Neurol* 2013; 260:1946-1947.
25. Shanthanna H, Busse J, Wang L, et al. Addition of corticosteroids to local anaesthetics for chronic non-cancer pain injections: A systematic review and meta-analysis of randomised controlled trials. *Br J Anaesth* 2020; 125:779-801.
26. Cyriax J. Epidural local anaesthesia. In: *Textbook of Orthopaedic Medicine*. Vol 1, 8th ed. Harcourt Publishers, New York, 1982, pp 310-27.
27. Evans W. Intrasacral epidural injection in the treatment of sciatica. *Lancet* 1930; 2:1225-1229.
28. Robecchi A, Capra R. Hydrocortisone (compound F); first clinical experiments in the field of rheumatology. *Minerva Med* 1952; 98:1259-1263.
29. Lievre JA, Bloch-Mechel H, Pean G. L'hydrocortisone en injection locale. *Rev Rhum* 1953; 20:310-311.
30. Manchikanti L, Kosanovic R, Vanaparthy R, et al. Steroid distancing in interventional pain management during COVID-19 and beyond: Safe, effective and practical approach. *Pain Physician* 2020; 23:S319-S350.
31. Tachihara H, Sekiguchi M, Kikuchi S, Konno S. Do corticosteroids produce additional benefit in nerve root infiltration for lumbar disc herniation. *Spine (Phila Pa 1976)* 2008; 33:743-747.
32. Manchikanti L, Knezevic E, Knezevic NN, et al. Epidural injections for lumbar radiculopathy or sciatica: A comparative systematic review and meta-analysis of Cochrane review. *Pain Physician* 2021; 24:E539-E554.
33. Wei G, Liang J, Chen B, et al. Comparison of transforaminal verse interlaminar epidural steroid injection in low back pain with lumbosacral radicular pain: A meta-analysis of the literature. *Int Orthop* 2016; 40:2533-2545.
34. Manchikanti L, Atluri S, Boswell MV, et al. Methodology for evidence synthesis and development of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. *Pain Physician* 2021; 24:S1-S26.
35. Furlan AD, Malmivaara A, Chou R, et al; Editorial Board of the Cochrane Back, Neck Group. 2015 updated method guideline for systematic reviews in the Cochrane Back and Neck Group. *Spine (Phila Pa 1976)* 2015; 40:1660-1673.
36. Manchikanti L, Hirsch JA, Cohen SP, et al. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. *Pain Physician* 2014; 17:E263-E290.
37. Manchikanti L, Falco FJE, Benyamin RM, Kaye AD, Boswell MV, Hirsch JA. A modified approach to grading of evidence. *Pain Physician* 2014; 17:E319-25.
38. Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. Effect of fluoroscopically guided caudal epidural steroid or local anesthetic injections in the treatment of lumbar disc herniation and radiculitis: A randomized, controlled, double blind trial with a two-year follow-up. *Pain Physician* 2012; 15:273-286.
39. Murakibhavi VG, Khemka AG. Caudal epidural steroid injection: A randomized controlled trial. *Evid Based Spine Care J* 2011; 2:19-26.
40. Manchikanti L, Singh V, Cash KA, Pampati V, Falco FJE. A randomized, double blind, active-control trial of the effectiveness of lumbar interlaminar epidural injections in disc herniation. *Pain Physician* 2014; 17:E61-E74.
41. Ghai B, Kumar K, Bansal D, Dhatt SS, Kanukula R, Batra YK. Effectiveness of parasagittal interlaminar epidural local anesthetic with or without steroid in chronic lumbosacral pain: A randomized, double-blind clinical trial. *Pain Physician* 2015; 18:237-248.
42. Ökmen K, Ökmen BM. The efficacy of interlaminar epidural steroid administration in multilevel intervertebral disc disease with chronic low back pain: A randomized, blinded, prospective study. *Spine J* 2017; 17:168-174.
43. Karppinen J, Malmivaara A, Kurunlahti M, et al. Periradicular infiltration for sciatica: A randomized controlled trial. *Spine (Phila Pa 1976)* 2001; 26:1059-1067.
44. Manchikanti L, Cash KA, Pampati V, Falco FJE. Transforaminal epidural injections in chronic lumbar disc herniation: A randomized, double-blind, active-control trial. *Pain Physician* 2014; 17:E489-E501.
45. Riew KD, Yin Y, Gilula L, et al. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain: A prospective, randomized, controlled, double-blind study. *J Bone Joint Surg Am* 2000; 82:1589-1593.
46. Riew D, Park JB, Cho YS, et al. Nerve root blocks in the treatment of lumbar radicular pain. A minimum five-year follow-up. *J Bone Joint Surg Am* 2006; 88:1722-1725.
47. 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; 18:1220-1225.
48. Ackerman WE 3rd, Ahmad M. The efficacy of lumbar epidural steroid injections in patients with lumbar disc herniations. *Anesth Analg* 2007; 104:1217-1222.
49. Dashfield A, Taylor M, Cleaver J, Farrow D. Comparison of caudal steroid epidural with targeted steroid placement during spinal endoscopy for chronic sciatica: A prospective, randomized, double-blind trial. *Br J Anaesth* 2005; 94:514-519.
50. Kamble PC, Sharma A, Singh V, Natraj B, Devani D, Khapane V. Outcome of single level disc prolapse treated with transforaminal steroid versus epidural steroid versus caudal steroids. *Eur Spine J* 2016; 25:217-221.
51. Pandey RA. Efficacy of epidural steroid injection in management of lumbar prolapsed intervertebral disc: A comparison of caudal, transforaminal and interlaminar routes. *J Clin Diagn Res* 2016; 10:RC05-11.
52. Singh S, Kumar S, Chahal G, Verma R. Selective nerve root blocks vs. caudal epidural injection for single level prolapsed lumbar intervertebral disc - A prospective randomized study. *J Clin Orthop Trauma* 2017; 8:142-147.
53. Rados I, Sakic K, Fingler M, Kapural L. Efficacy of interlaminar vs transforaminal epidural steroid injection for the treatment of chronic unilateral radicular pain: Prospective, randomized study. *Pain Med* 2011;

12:1316-1321.

54. Ghai B, Bansal D, Kay JP, Vadaje KS, Wig J. Transforaminal versus parasagittal interlaminar epidural steroid injection in low back pain with radicular pain: A randomized, double-blind, active-control trial. *Pain Physician* 2014; 17:277-290.
55. Candido KD, Rana MV, Sauer R, et al. Concordant pressure paresthesia during interlaminar lumbar epidural steroid injections correlates with pain relief in patients with unilateral radicular pain. *Pain Physician* 2013; 16:497-511.
56. Amr YM. Effect of addition of epidural ketamine to steroid in lumbar radiculitis: One-year follow-up. *Pain Physician* 2011; 14:475-481.
57. Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: A prospective randomized study. *Spine (Phila Pa 1976)* 2002; 27:11-16.
58. Jeong HS, Lee JW, Kim SH, Myung JS, Kim JH, Kang HS. Effectiveness of transforaminal epidural steroid injection by using a preganglionic approach: A prospective randomized controlled study. *Radiology* 2007; 245:584-590.
59. Kennedy D, Plastaras C, Casey E, et al. Comparative effectiveness of lumbar transforaminal epidural steroid injections with particulate versus nonparticulate corticosteroids for lumbar radicular pain due to intervertebral disc herniation: A prospective, randomized, double-blind trial. *Pain Med* 2014; 15:548-555.
60. Karppinen J, Ohinmaa A, Malmivaara A, et al. Cost effectiveness of periradicular infiltration for sciatica: Subgroup analysis of a randomized controlled trial. *Spine (Phila Pa 1976)* 2001; 26:2587-2595.
61. Mesregah MK, Feng W, Huang WH, et al. Clinical effectiveness of interlaminar epidural injections of local anesthetic with or without steroids for managing chronic neck pain: A systematic review and meta-analysis. *Pain Physician* 2020; 23:335-348.
62. Eden J, Levit L, Berg A, Morton S (eds); Committee on Standards for Systematic Reviews of Comparative Effectiveness Research; Institute of Medicine. Finding What Works in Health Care. Standards for Systematic Reviews. The National Academies Press, Washington, DC, 2011. Accessed 2/19/2021. www.nap.edu/catalog/13059/finding-what-works-in-health-carestandards-for-systematic-reviews
63. Cappola AR, FitzGerald GA. Confluence, not conflict of interest: Name change necessary. *JAMA* 2015; 314:1791-1792.
64. Manchikanti L, Kaye AD, Soin A, et al. Comprehensive evidence-based guidelines for facet joint interventions in the management of chronic spinal pain: American Society of Interventional Pain Physicians (ASIPP) guidelines. *Pain Physician* 2020; 23:S1-S127.
65. Manchikanti L, Knezevic NN, Sanapati SP, Sanapati MR, Kaye AD, Hirsch JA. Is percutaneous adhesiolysis effective in managing chronic low back and lower extremity pain in post-surgery syndrome: A systematic review and meta-analysis. *Curr Pain Headache Rep* 2020; 24:30.
66. Manchikanti L, Knezevic NN, Sanapati MR, Boswell MV, Kaye AD, Hirsch JA. Effectiveness of percutaneous adhesiolysis in managing chronic central lumbar spinal stenosis: A systematic review and meta-analysis. *Pain Physician* 2019; 22:E523-E550.
67. Manchikanti L, Soin A, Boswell MV, Kaye AD, Sanapati M, Hirsch JA. Effectiveness of percutaneous adhesiolysis in post lumbar surgery syndrome: A systematic analysis of findings of systematic reviews. *Pain Physician* 2019; 22:307-322.

Appendix Table 1. ***Methodological quality assessment of randomized trials of epidural injections in lumbar disc herniation utilizing Cochrane review criteria.***

	Manchikanti et al (38)	**Ackerman & Ahmad (48)**	**Dashfield et al (49)**	**Murakibhavi & Khemka (39)**	**Kamble et al (50)**	**Pandey (51)**	**Singh et al (52)**	**Manchikanti et al (40)**
Randomization adequate	Y	N	Y	Y	Y	N	N	Y
Concealed treatment allocation	Y	N	Y	N	Y	N	N	Y
Patient blinded	Y	N	Y	Y	Y	N	N	Y
Care provider blinded	Y	N	N	N	N	N	N	Y
Outcome assessor blinded	N	N	N	N	Y	N	N	N
Drop-out rate described	Y	Y	Y	Y	N	Y	Y	Y
All randomized participants analyzed in the group	Y	Y	Y	Y	N	Y	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	Y	Y	Y	N	Y	Y	Y	N
Co-interventions avoided or similar	Y	Y	N	N	Y	Y	Y	Y
Compliance acceptable in all group	Y	Y	Y	Y	U	Y	Y	Y
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y	Y	Y	Y
Are other sources of potential bias likely	Y	Y	Y	Y	Y	Y	Y	Y
Score	12/13	8/13	10/13	8/13	9/13	8/13	8/13	11/13

	Ghai et al (41)	**Ökmen & Ökmen (42)**	**Rados et al (53)**	**Ghai et al (54)**	**Candido et al (55)**	**Amr (56)**	**Karppinen et al (43)**	**Manchikanti et al (44)**
Randomization adequate	Y	Y	Y	Y	Y	Y	Y	Y
Concealed treatment allocation	Y	Y	N	Y	Y	Y	Y	Y
Patient blinded	Y	Y	N	N	N	Y	Y	Y
Care provider blinded	N	Y	N	N	N	Y	Y	Y
Outcome assessor blinded	N	Y	N	N	N	Y	Y	N
Drop-out rate described	N	Y	Y	Y	Y	Y	Y	Y
All randomized participants analyzed in the group	Y	N	Y	Y	Y	N	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	Y	Y	Y	Y	Y	Y	Y	N
Co-interventions avoided or similar	Y	Y	Y	Y	Y	Y	Y	Y
Compliance acceptable in all group	Y	Y	Y	Y	Y	Y	Y	Y
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y	Y	Y	Y
Are other sources of potential bias likely	Y	Y	Y	Y	Y	Y	Y	Y
Score	10/13	12/13	9/13	10/13	10/13	12/13	13/13	11/13

Appendix Table 1 (cont.). ***Methodological quality assessment of randomized trials of epidural injections in lumbar disc herniation utilizing Cochrane review criteria.***

	Riew et al (45,46)	**Tafazal et al (47)**	**Vad et al (57)**	**Jeong et al (58)**	**Kennedy et al (59)**
Randomization adequate	U	Y	U	U	Y
Concealed treatment allocation	U	Y	N	U	Y
Patient blinded	Y	Y	N	Y	N
Care provider blinded	N	Y	N	N	N
Outcome assessor blinded	Y	N	U	Y	N
Drop-out rate described	Y	Y	N	Y	Y
All randomized participants analyzed in the group	Y	N	N	Y	Y
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	U	Y	Y	Y	Y
Co-interventions avoided or similar	Y	Y	Y	Y	Y
Compliance acceptable in all group	Y	Y	U	Y	Y
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y
Are other sources of potential bias likely	Y	Y	Y	Y	Y
Score	9/13	11/13	5/13	10/13	10/13

Y = Yes; N = No; U = Unclear

Adapted from: Manchikanti L, et al. Epidural injections for lumbar radiculopathy or sciatica: A comparative systematic review and meta-analysis of Cochrane review. *Pain Physician* 2021; 24:E539-E554 (32).

Source: Furlan AD, Malmivaara A, Chou R, Maher CG, Deyo RA, Schoene M, Bronfort G, van Tulder MW; Editorial Board of the Cochrane Back, Neck Group. 2015 Updated Method Guideline for Systematic Reviews in the Cochrane Back and Neck Group. *Spine (Phila Pa 1976)* 2015; 40:1660-1673 (35).

Appendix Table 2. *Methodologic quality assessment of randomized trials of epidural injections in lumbar disc herniation utilizing IPM – QRB.*

		Manchikanti et al (38)	Ackerman & Ahmad (48)	Dashfield et al (49)	Murakibhavi & Khemka (39)	Kamble et al (50)	Pandey (51)	Singh et al (52)	Manchikanti et al (40)
I.	TRIAL DESIGN AND GUIDANCE REPORTING								
1.	CONSORT or SPIRIT	3	0	1	2	0	0	1	3
II.	DESIGN FACTORS								
2.	Type and Design of Trial	2	2	2	2	2	2	2	2
3.	Setting/Physician	2	2	2	1	2	2	2	2
4.	Imaging	3	3	3	3	2	2	3	3
5.	Sample Size	3	1	1	2	2	1	2	3
6.	Statistical Methodology	1	1	1	1	1	1	1	1
III.	PATIENT FACTORS								
7.	Inclusiveness of Population	2	2	1	2	2	2	2	2
8.	Duration of Pain	2	1	2	1	1	2	2	2
9.	Previous Treatments	2	0	0	0	2	2	2	2
10.	Duration of Follow-up with Appropriate Interventions	3	2	2	1	1	2	1	3
IV.	OUTCOMES								
11.	Outcomes Assessment Criteria for Significant Improvement	4	1	2	4	2	2	2	4
12.	Analysis of all Randomized Participants in the Groups	2	2	2	2	2	2	2	2
13.	Description of Drop Out Rate	2	2	2	2	0	2	2	2
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	1	1	1	0	1	1	1	1
15.	Role of Co-Interventions	1	1	1	0	1	1	1	1
V.	RANDOMIZATION								
16.	Method of Randomization	2	0	2	0	2	0	0	2
VI.	ALLOCATION CONCEALMENT								
17.	Concealed Treatment Allocation	2	0	2	2	2	0	0	2
VII.	BLINDING								
18.	Patient Blinding	1	0	1	1	1	0	0	1
19.	Care Provider Blinding	1	0	0	0	0	0	0	1
20.	Outcome Assessor Blinding	0	0	0	0	1	0	0	0
VIII.	CONFLICTS OF INTEREST								
21.	Funding and Sponsorship	2	1	2	0	2	2	2	2
22.	Conflicts of Interest	3	3	3	1	3	3	2	3
TOTAL		44	25	33	27	32	29	30	44

Appendix Table 2 (cont.). ***Methodologic quality assessment of randomized trials of epidural injections in lumbar disc herniation utilizing IPM – QRB.***

		Ghai et al (41)	Ökmen & Ökmen (42)	Rados et al (53)	Ghai et al (54)	Candido et al (55)	Amr (56)	Karppinen et al (43)	Manchikanti et al (44)
I.	TRIAL DESIGN AND GUIDANCE REPORTING								
1.	CONSORT or SPIRIT	3	2	2	3	2	2	2	3
II.	DESIGN FACTORS								
2.	Type and Design of Trial	2	2	2	2	2	2	2	2
3.	Setting/Physician	2	2	3	2	2	3	1	2
4.	Imaging	3	3	3	3	3	3	3	3
5.	Sample Size	2	3	1	2	2	3	3	3
6.	Statistical Methodology	1	1	1	1	1	1	1	1
III.	PATIENT FACTORS								
7.	Inclusiveness of Population	2	2	1	2	2	2	2	2
8.	Duration of Pain	1	2	2	2	1	2	0	2
9.	Previous Treatments	1	2	0	2	2	2	0	2
10.	Duration of Follow-up with Appropriate Interventions	3	2	2	3	2	3	1	3
IV.	OUTCOMES								
11.	Outcomes Assessment Criteria for Significant Improvement	4	2	2	4	2	2	2	4
12.	Analysis of all Randomized Participants in the Groups	2	1	2	2	2	1	2	2
13.	Description of Drop Out Rate	0	2	2	2	2	2	1	2
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	2	2	2	2	2	2	2	1
15.	Role of Co-Interventions	1	1	1	1	1	1	0	1
V.	RANDOMIZATION								
16.	Method of Randomization	2	2	2	2	2	2	2	2
VI.	ALLOCATION CONCEALMENT								
17.	Concealed Treatment Allocation	2	2	0	2	2	2	2	2
VII.	BLINDING								
18.	Patient Blinding	1	1	0	0	0	1	1	1
19.	Care Provider Blinding	0	0	0	0	0	1	1	1
20.	Outcome Assessor Blinding	0	1	0	0	0	1	1	0
VIII.	CONFLICTS OF INTEREST								
21.	Funding and Sponsorship	2	2	0	2	2	0	2	2
22.	Conflicts of Interest	3	3	2	3	3	0	3	3
TOTAL		39	40	30	42	37	38	34	44

Appendix Table 2 (cont.). ***Methodologic quality assessment of randomized trials of epidural injections in lumbar disc herniation utilizing IPM – QRB.***

		Riew et al (45,46)	**Tafazal et al (47)**	**Vad et al (57)**	**Jeong et al (58)**	**Kennedy et al (59)**
I.	TRIAL DESIGN AND GUIDANCE REPORTING					
1.	CONSORT or SPIRIT	1	2	1	2	3
II.	DESIGN FACTORS					
2.	Type and Design of Trial	2	2	2	2	2
3.	Setting/Physician	1	1	1	1	2
4.	Imaging	3	3	2	3	3
5.	Sample Size	2	1	1	3	2
6.	Statistical Methodology	1	1	1	1	1
III.	PATIENT FACTORS					
7.	Inclusiveness of Population	2	1	2	1	2
8.	Duration of Pain	1	1	0	0	0
9.	Previous Treatments	2	2	0	0	2
10.	Duration of Follow-up with Appropriate Interventions	2	1	1	2	1
IV.	OUTCOMES					
11.	Outcomes Assessment Criteria for Significant Improvement	1	2	2	2	2
12.	Analysis of all Randomized Participants in the Groups	2	1	0	2	2
13.	Description of Drop Out Rate	2	1	0	2	1
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	2	1	0	2	2
15.	Role of Co-Interventions	0	1	1	1	1
V.	RANDOMIZATION					
16.	Method of Randomization	1	2	0	1	2
VI.	ALLOCATION CONCEALMENT					
17.	Concealed Treatment Allocation	0	2	0	0	2
VII.	BLINDING					
18.	Patient Blinding	1	1	0	1	0
19.	Care Provider Blinding	1	1	0	0	0
20.	Outcome Assessor Blinding	0	0	0	1	0
VIII.	CONFLICTS OF INTEREST					
21.	Funding and Sponsorship	2	2	0	2	0
22.	Conflicts of Interest	3	3	2	2	0
TOTAL		32	32	16	31	30

Adapted from: Manchikanti L, et al. Epidural injections for lumbar radiculopathy or sciatica: A comparative systematic review and meta-analysis of Cochrane review. *Pain Physician* 2021; 24:E539-E554 (32).
Source: Manchikanti L, et al. Assessment of methodologic quality of randomized trials of interventional techniques: Development of an interventional pain management specific instrument. *Pain Physician* 2014; 17:E263-E290 (36).

Appendix Table 3. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Karppinen et al, 2001 (43) RA, PC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 13/13 IPM-QRB = 34/48	Total=160 Methylprednisolone-bupivacaine = 80 Saline = 80 Sodium chloride solution, or methylprednisolone (40 mg) and bupivacaine (5 mg) Number of injections = 1	VAS, ODI, Nottingham Health Profile, cost, physical examination Follow-up: 12 months with only initial procedures	A significant treatment effect in favor of saline treatment for back pain.	The treatment effects in both leg pain and back pain favored the saline treatment.	There were no treatment effects in favor of either treatment.	NA	Lack of effectiveness of steroid with bupivacaine	Lack of effectiveness of steroid with bupivacaine	Lack of effectiveness of steroid with bupivacaine	NA	• An ineffective or inappropriate placebo design, without applicable results. • Overall saline appears to have been superior at 3 months and 6 months, but no significant difference at one year between both groups. • Leg pain decreased on average by 65% in both groups. • Surgery was avoided in the majority of the patients with 18 patients in the steroid group and 15 in the saline group undergoing surgery.
Manchikanti et al, 2014 (44) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 11/13 IPM-QRB = 44/48	Total = 120 Lidocaine = 60 Lidocaine with steroids = 60 Lidocaine vs lidocaine mixed with steroid with infraneural approach Average number of injections = 5 to 6 for 2 years	NRS pain scale, ODI, employment status, opioid intake Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 75% vs LA with steroid 67% Responsive: LA 90% vs LA with steroid 82%	Overall: LA 73% vs LA with steroid 67% Responsive LA 88% vs LA with steroid 87%	Overall: LA 75% vs LA with steroid 57% Responsive LA 92% vs LA with steroid 73%	Overall: LA 65% vs LA with steroid 57% Responsive LA 80% vs LA with steroid 73%	Effectiveness in both groups. Lidocaine alone or with steroids effective.	Effectiveness in both groups. Lidocaine alone or with steroids effective.	Effectiveness in both groups. Lidocaine alone or with steroids effective.	Effectiveness in both groups. Lidocaine alone or with steroids effective.	• Similar results with local anesthetic or with local anesthetic and steroids. • Nonresponsive patients: local anesthetic = 11, steroids = 15. • Local anesthetics were somewhat superior, though not statistically significant. • On average, a total of 5-6 injections were administered over a period of 2 years.
Riew et al, 2000 & 2006 (45,46) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Total = 55 Bupivacaine alone (1 mL, 0.25%)=27 Bupivacaine (1 mL, 0.25%) with steroid (1 mL betamethasone)=28 Number of injections = 1-4	Need for operative treatment, North American Spine Society Questionnaire Follow-up: 1 months to 28 months	71% of steroid group chose not to have surgery and 33% of bupivacaine group chose not to have surgery	71% of steroid group chose not to have surgery and 33% of bupivacaine group chose not to have surgery	71% of steroid group chose not to have surgery and 33% of bupivacaine group chose not to have surgery	NA	*P*	*P*	*P*	NA	• Epidural bupivacaine with steroids was significantly more effective than transforaminal bupivacaine with steroids was significantly more effective than epidural bupivacaine alone in avoiding surgery.

Appendix Table 3 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Tafazal et al, 2009 (47) RA, AC, F Disc herniation or radiculopathy and spinal stenosis Quality Scores: Cochrane = 11/13 IPM-QRB = 32/48	Total: 150 patients Lumbar disc herniation: 76 Local anesthetic = 34 Local anesthetic with steroid = 42 Local anesthetic group: Injection of 2 mL of 0.25% bupivacaine Local anesthetic with steroid group: Injection of 2 mL of 0.25% bupivacaine and 40 mg of methylprednisolone. Bupivacaine only: Lumbar disc herniation: 34 Foraminal stenosis: 25 Bupivacaine with steroids Lumbar disc herniation: 42 Foraminal stenosis: 23 Number of injections = 1 to 3	VAS, ODI, LBOS Avoidance of surgery Outcomes: 12 weeks 1 year for surgery Excellent outcome	ODI: LA 13.8 ± 3.7 versus LA with steroid 13.6 ± 3.1 VAS leg pain: LA 24.3 ± 5.5 versus LA with steroid 27.4.6 ± 4.7	NA	Disc herniation group showed greater reduction in the ODI with a mean change of 15 points from baseline of 46.6 in the bupivacaine only group and 43.4 in bupivacaine and steroid group. There was a mean change in the VAS of 26 mm in the disc prolapse group.	NA	Excellent to good outcomes in 54% Bupivacaine alone and bupivacaine with steroid are both effective	NA	The requirements for treatments were the same in local anesthetic alone group or local anesthetic with steroids. Overall surgery rates was 18%, the surgery rate was 22% in the bupivacaine only group and 14% in the bupivacaine and steroid group.	NA	• Corticosteroid addition to local anesthetic failed to provide any additional benefit when compared to local anesthetic injection alone. • There was no significant difference between both groups. Surgery was avoided in both groups.
Ackerman & Ahmad, 2007 (48) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	NA	NA	Effective in all arms	Effective in all arms	NA	NA	Positive mid-term results in a relatively small trial.

Appendix Table 3 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar disc herniation.*

Study **Study Characteristics** **Methodological Quality Scoring**	**Participants and Interventions**	**Outcome Measures**	**Pain Relief and Function**				**Results**				**Comment(s)**
								Long-Term			
			3 mos.	**6 mos.**	**12 mos.**	**24 mos.**	**Short-term ≤ 6 mos.**	**> 6 mos.**	**≥ 12 mos.**	**24 mos.**	
Kamble et al, 2016 (50) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	NA	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	NA	NA	All 3 techniques were effective	NA	NA	NA	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.
Pandey, 2016 (51) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	NA	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	NA	*P*	*P*	*P*	NA	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.

Appendix Table 3 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
								Long-Term			
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term $\leq$ 6 mos.	> 6 mos.	$\geq$ 12 mos.	24 mos.	
Rados et al, 2011 (53) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 9/13 IPM-QRB = 30/48	Total = 64 IL = 32 TF = 32 Lidocaine with methylprednisolone Number of injections = 1 to 3	VAS, ODI, 50% pain relief Follow-up: 6 months	NA	Interlaminar lidocaine with methylprednisolone = 53% Transforaminal lidocaine with methylprednisolone = 63%	NA	NA	Effective with both approaches	NA	NA	NA	• Positive results with short follow-up period in comparison of 2 approaches with lidocaine with methylprednisolone
Ghai et al, 2014 (54) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 42/48	Total = 62 Parasagittal interlaminar = 32 Transforaminal = 30 2 mL of methylprednisolone (80 mg) mixed with 2 mL of normal saline for both PIL and transforaminal groups Number of epidural steroid injections: Transforaminal group: 60 PIL group: 58 Average procedures: 2	Visual analog scale, Oswestry Disability questionnaire, significant improvement, greater than 50% pain relief from baseline, Patient Global Impression	PIL group: 78% Transforaminal group: 77%	PIL group: 75% Transforaminal group: 77%	PIL group: 69% Transforaminal group: 77%	NA	Effectiveness in both arms	Effectiveness in both arms	Effectiveness in both arms	NA	This is relatively small active control trial with a long-term follow-up assessing the role of parasagittal interlaminar epidural injections and transforaminal epidural injections showing equal improvement with steroids without local anesthetic.
Vad et al, 2002 (57) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 5/13 IPM-QRB = 16/48	Total: 50 patients Transforaminal: 25 Trigger point injections: 25 Transforaminal injections were performed by safe triangle approach or sacral foramen injection utilizing contrast followed by 1.5 mL of betamethasone acetate 9 mg and 1.5 mL of 2% preservative free Xylocaine. Trigger point injections were performed with 3 mL of normal saline	Outcome measures included visual numeric score, Roland-Morris score, finger to floor distance, and patient satisfaction score. Outcomes were measured at 3 weeks, 6 weeks, 3 months, 6 months, and 12 months.	In transforaminal group 84% showed improvement in trigger point injection group 48% showed improvement	In transforaminal group 84% showed improvement. in trigger point injection group 48% showed improvement	In transforaminal group 84% showed improvement in trigger point injection group 48% showed improvement.	NA	Transforaminal steroids with lidocaine effective	Transforaminal steroids with lidocaine effective	Transforaminal steroids with lidocaine effective	NA	This is a randomized trial, but randomization was by patient choice with patients receiving either a high dose transforaminal epidural steroid injection or saline trigger point injection. Study yielded positive results for transforaminal epidural injections at one-year follow-up.

Appendix Table 3 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
							Short-term	Long-Term			
			3 mos.	6 mos.	12 mos.	24 mos.	≤ 6 mos.	> 6 mos.	≥ 12 mos.	24 mos.	
Jeong et al, 2007 (58) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 31/48	Total=193 Ganglionic = 104 Preganglionic = 89 0.5 mL of bupivacaine hydrochloride and 40 mg of 1 mL of triamcinolone Number of injections = 1	VAS Follow-up: 7-30 days 6 months	Preganglionic = 88.4% Ganglionic = 70.9%	Preganglionic = 60.4% Ganglionic = 67.2%	NA	NA	Both approaches effective	Both approaches effective	NA	NA	Moderate quality study with mid-term positive results.
Kennedy et al, 2014 (59) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 30/48	Total patients = 78 Dexamethasone 15 mg or 1.5 mL = 41 patients Triamcinolone 60 mg or 1.5 mL = 37 patients Number of Injections: 1 to 3	NRS, ODI, at least 50% reduction in pain and disability scores	Dexamethasone group 73% reduction in pain scores, 68% reduction in ODI scores Triamcinolone group 73% reduction in pain scores, 68% reduction in ODI scores	Dexamethasone group 73% reduction in pain scores, 71% reduction in ODI scores Triamcinolone group 76% reduction in pain scores, 65% reduction in ODI scores	NA	NA	Both drugs effective	Both drugs effective	NA	NA	In this comparative assessment of dexamethasone 15 mg with triamcinolone 60 mg, there was no significant difference with pain or functionality at 6 months.

RA = Randomized; AC = Active Control; F = Fluoroscopy; PC = Placebo-control; IPM-QRB = Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment; NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; VAS = Visual Analog Scale; BDI = Beck Depression Inventory; NPI = Numerical Pain Intensity; LBOS = Low Back Outcome Score; JOA – Japanese Orthopaedic Association; PIL = Parasagittal Interlaminar; LA = local anesthetic; NA = Not Applicable; P = Positive

Adapted from: Manchikanti L, et al. Epidural injections for lumbar radiculopathy or sciatica: A comparative systematic review and meta-analysis of Cochrane review. Pain Physician 2021; 24:E539-E554 (32).

Appendix Table 4. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
								Long-Term			
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	> 6 mos.	≥ 12 mos.	24 mos.	
Manchikanti et al, 2014 (40) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 11/13 IPM-QRB = 44/48	Total = 120 Local anesthetic = 60 Local anesthetic and steroids = 60 Xylocaine or Xylocaine with non-particulate Celestone Average number of injections = 5 to 6 for 2 years	NRS, ODI, employment status, opioid intake, significant improvement 50% or greater of NRS scores and ODI scores Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: Lidocaine 72% vs. lidocaine with steroid 82% Responsive: Lidocaine 86% vs. lidocaine with steroid 83%	Overall: Lidocaine 63% vs. lidocaine with steroid 85% Responsive: Lidocaine 76% vs. lidocaine with steroid 86%	Overall: Lidocaine 67% vs. lidocaine with steroid 85% Responsive: Lidocaine 80% vs. lidocaine with steroid 86%	Overall: Lidocaine 60% vs lidocaine with steroid 70% Responsive: Lidocaine 72% vs. lidocaine with steroid 71%	Both treatments are effective	Both treatments are effective	Both treatments are effective	Both treatments are effective	• Positive randomized trial with long-term follow-up. • Overall, similar results with local anesthetic or with local anesthetic and steroids with significant improvement. • Steroids were superior at 6 months with pain relief and 12 months with functional status • A significantly higher proportion of patients non-responsive to the first 2 injections in the local anesthetic group 10 vs one. • On average, a total of 5-6 injections were provided over a period of 2 years.
Ghai et al, 2015 (41) RA, DB, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 39/48	Total = 69 Lidocaine = 34 Lidocaine + methylprednisolone = 35 Local anesthetic group: 8 mL of 0.5% lidocaine Lidocaine + methylprednisolone: 6 ml of 0.5% lidocaine mixed with 80 mg (2 mL) of methylprednisolone acetate Average procedures: 2	NRS and functional disability using Modified Oswestry Disability Questionnaire Follow-up: 1 year	Lidocaine: 50% Lidocaine with methylprednisolone: 86%	Lidocaine: 56% Lidocaine with methylprednisolone: 86%	Lidocaine: 59% Lidocaine with methylprednisolone: 89%	NA	Both arms effective. Steroids superior	Both arms effective. Steroids superior	Both arms effective. Steroids superior	NA	This active control trial with a long-term follow-up comparing lidocaine alone with lidocaine with methylprednisolone showed similar results after 3 months, even though quality of relief was superior in the local anesthetic with steroid group.

Appendix Table 4 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term			
								> 6 mos.	≥ 12 mos.	24 mos.	
Ökmen & Ökmen 2017 (42) RA, AC, F Disc herniation Quality Scores: Cochrane = 12/13 IPM-QRB = 40/48	Total = 120 Epidural bupivacaine 0.25%, 10 mL = 60 Epidural bupivacaine 0.25%, 10 mL + 40 mg of methylprednisolone = 60 Procedures administered at L4-5 under fluoroscopic guidance Number of injections = 1-2	VAS, ODI Follow-up: 1 to 12 months	Significantly better results in epidural bupivacaine and steroid group Both groups showed significant improvement from baseline, more significant in the steroid group than bupivacaine alone group.	Significantly better results in epidural bupivacaine and steroid group Both groups showed significant improvement from baseline, more significant in the steroid group than bupivacaine alone group.	Significantly better results in epidural bupivacaine and steroid group Both groups showed significant improvement from baseline, more significant in the steroid group than	NA	Bupivacaine steroids superior	Bupivacaine steroids superior	Bupivacaine steroids superior	NA	• Positive results for both epidural bupivacaine and epidural bupivacaine with steroids. • Significant improvement in epidural bupivacaine and steroid group from baseline with pain and function, as well as ODI compared to bupivacaine.
Ackerman & Ahmad, 2007 (48) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	NA	NA	Effective in all arms	Effective in all arms	NA	NA	Positive mid-term results in a relatively small trial.

Appendix Table 4 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Kamble et al, 2016 (50) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	NA	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	NA	NA	All 3 techniques were effective	NA	NA	NA	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.
Pandey, 2016 (51) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	NA	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	NA	P	P	P	NA	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.

Appendix Table 4 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
								Long-Term			
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	> 6 mos.	≥ 12 mos.	24 mos.	
Rados et al, 2011 (53) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 9/13 IPM-QRB = 30/48	Total = 64 IL = 32 TF = 32 Lidocaine with methylprednisolone Number of injections = 1 to 3	VAS, ODI, 50% pain relief Follow-up: 6 months	NA	Interlaminar lidocaine with methylprednisolone = 53% Transforaminal lidocaine with methylprednisolone = 63%	NA	NA	Effective with both approaches	NA	NA	NA	• Positive results with short follow-up period in comparison of 2 approaches with lidocaine with methylprednisolone
Ghai et al, 2014 (54) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 42/48	Total = 62 Parasagittal interlaminar = 32 Transforaminal = 30 2 mL of methylprednisolone (80 mg) mixed with 2 mL of normal saline for both PIL and transforaminal groups Number of epidural steroid injections: Transforaminal group: 60 PIL group: 58 Average procedures: 2	Visual analog scale, Oswestry Disability questionnaire, significant improvement, greater than 50% pain relief from baseline, Patient Global Impression	PIL group: 78% Transforaminal group: 77%	PIL group: 75% Transforaminal group: 77%	PIL group: 69% Transforaminal group: 77%	NA	Effectiveness in both arms	Effectiveness in both arms	Effectiveness in both arms	NA	This is relatively small active control trial with a long-term follow-up assessing the role of parasagittal interlaminar epidural injections and transforaminal epidural injections showing equal improvement with steroids without local anesthetic.
Candido et al, 2013 (55) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 37/48	106 patients Midline interlaminar = 53 Parasagittal interlaminar = 53 120 mg methylprednisolone with 2 mL of 0.5% lidocaine Number of Injections: Not available	Pain relief, disability, NRS, ODI, use of opioid medication Follow-up: 12 months	ODI Midline = 36% Parasagittal = 51% Pain: Midline = 29% Parasagittal = 50%	ODI Midline = 21% Parasagittal = 55% Pain: Midline = 29% Parasagittal = 53%	ODI Midline = 15% Parasagittal = 56% Pain: Midline = 28% Parasagittal = 55%	NA	Parasagittal superior	Parasagittal superior	Parasagittal superior	NA	• The authors showed significant evidence that parasagittal approach with injection of local anesthetic and steroids was superior to midline approach of interlaminar epidural injections. • This study shows combination of methylprednisolone with lidocaine was superior administered with a parasagittal approach compared to midline approach.

Appendix Table 4 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
								Long-Term			
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	> 6 mos.	≥ 12 mos.	24 mos.	
Amr, 2011 (56) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 12/13 IPM-QRB = 38/48	Total = 200 Local anesthetic + steroid = 100 Local anesthetic + steroid + ketamine = 100 Triamcinolone plus preservative free ketamine and 0.9% saline Number of injections = 1	Pain scores, Oswestry low back pain disability questionnaire	Significant improvement in ketamine group	Significant improvement in ketamine group	Significant improvement in ketamine group	NA	Effective with addition of ketamine to bupivacaine and triamcinolone	Effective with addition of ketamine to bupivacaine and triamcinolone	Effective with addition of ketamine to bupivacaine and triamcinolone	NA	• Positive randomized trial for ketamine with long-term follow-up with ketamine with local anesthetic and steroid.

RA = Randomized; AC = Active Control; F = Fluoroscopy; DB = Double-Blind; IPM-QRB = Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment; NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; VAS = Visual Analog Scale; BDI = Beck Depression Inventory; NPI = Numerical Pain Intensity; JOA – Japanese Orthopaedic Association; NA = Not Applicable; IL = interlaminar; TF = transforaminal

Adapted from: Manchikanti L, et al. Epidural injections for lumbar radiculopathy or sciatica: A comparative systematic review and meta-analysis of Cochrane review. Pain Physician 2021; 24:E539-E554 (32).

Appendix Table 5. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in caudal epidural injections in lumbar disc herniation.*

Study **Study Characteristics** **Methodological Quality Scoring**	**Participants and Interventions**	**Outcome Measures**	**Pain Relief and Function**				**Results**				**Comment(s)**
			3 mos.	**6 mos.**	**12 mos.**	**24 mos.**	**Short-term ≤ 6 mos.**	**Long-Term**			
								> 6 mos.	**≥ 12 mos.**	**24 mos.**	
Manchikanti et al, 2012 (38) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 12/13 IPM-QRB = 44/48	Total = 120 Lidocaine = 60 Lidocaine with steroids = 60 Lidocaine vs. lidocaine mixed with steroid Number of injections = 1 to 5	NRS, ODI, employment status, opioid intake Responsive category was defined as at least 3 weeks of significant improvement with the first 2 procedures. Significant improvement: 50% improvement in pain and function.	Overall: LA 62% vs. LA with steroid 72% Responsive: LA 77% vs LA with steroid 80%	Overall: LA 72% vs LA with steroid 73% Responsive: LA 87% vs LA with steroid 86%	Overall: LA 67% vs LA with steroid 72% Responsive: LA 85% vs LA with steroid 84%	Overall: LA 60% vs LA with steroid 65% Responsive: LA 77% vs LA with steroid 76%	Lidocaine & lidocaine with steroid effective	Lidocaine & lidocaine with steroid effective	Lidocaine & lidocaine with steroid effective	Lidocaine & lidocaine with steroid effective	• Positive double-blind randomized trial with superiority of steroids with average pain relief for steroids. Overall improvement with local anesthetic alone or with steroids was similar. • Nonresponsive patients were also similar with 13 and 10 in local anesthetic only and with steroids group. • Over a period of 2 years, on average, a total of 5-6 injections were provided.
Murakibhavi & Khemka, 2011 (39) RA, NTC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 27/48	Group A = 50 control conservative management Group B = 52 caudal epidural with lidocaine and methylprednisolone Total = 102 patients Conservative management or caudal epidural steroid injections	VAS, ODI, BDI, NPI	Group A = 32% Group B = 92%	Group A = 24% Group B = 86%	NA	NA	Steroids effective	Steroids effective	NA	NA	Positive short-term results, with methylprednisolone and lidocaine.
Ackerman & Ahmad, 2007 (48) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	NA	NA	Effective in all arms	Effective in all arms	NA	NA	Positive mid-term results in a relatively small trial.

Appendix Table 5 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in caudal epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Dashfield et al, 2005 (49) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 33/48	Total = 60 Caudal = 30 Endoscopy =30 Lidocaine with triamcinolone Number of injections = 1	Pain relief, SF-MPQ, HADS scores	SI	SI	NA	NA	Lidocaine with triamcinolone effective	Lidocaine with triamcinolone effective	NA	NA	Positive mid-term results in a relatively small trial.
Kamble et al, 2016 (50) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	NA	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	NA	NA	All 3 techniques were effective	NA	NA	NA	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.

Appendix Table 5 (cont.). *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in caudal epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Pandey, 2016 (51) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	NA	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	NA	*P*	*P*	*P*	NA	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.
Singh et al, 2017 (52) RA, AC, F Single level prolapsed lumbar intervertebral disc Quality Scores: Cochrane = 8/13 IPM-QRB = 30/48	Number of patients = 80 Caudal with steroids group = 40 2 mL of methylprednisolone, 80 mg along with lignocaine 2% diluted in 20 mL of normal saline 3 caudal epidural injections were given at an interval of 3 weeks irrespective of previous epidural injection effect SNRB = 40 A single injection of 2 mL of methylprednisolone, 80 mg, mixed with 5 mL of lignocaine 2%	VAS, ODI & significant pain relief of 50%	VAS Caudal vs. SNRB = 61.5% vs. 55.5% ODI decreased caudal vs. SNRB = 64.6% vs. 52.8%	VAS Caudal vs. SNRB= 59.6% vs. 52.9% ODI decreased caudal vs. SNRB = 65.1% vs. 48.6%	VAS Caudal vs. SNRB= 58.2% vs. 46.8% ODI decreased caudal vs. SNRB = 65.4% vs. 46.7%	NA	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Positive short-term and long-term relief in both caudal and SNRB; however, relief in the caudal group was superior. However, this study suffered with multiple limitations of 3 caudal epidural injections compared to one SNRB and high volumes of injections, which are clinically inappropriate in both caudal and SNRB groups.

RA = Randomized; AC = Active Control; F = Fluoroscopy; NTC = No treatment control; IPM-QRB = Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment; NRS = Numeric Rating Scale; ODI = Oswestry Disability Index; VAS = Visual Analog Scale; BDI = Beck Depression Inventory; NPI = Numerical Pain Intensity; SF-MPQ = Short-Form McGill Pain Questionnaire; HADS = Hospital Anxiety and Depression Scale; JOA – Japanese Orthopaedic Association; SNRB = Selective nerve root block; LA = local anesthetic; NA = Not Applicable; SI = Significant improvement
Adapted from: Manchikanti L, et al. Epidural injections for lumbar radiculopathy or sciatica: A comparative systematic review and meta-analysis of Cochrane review. Pain Physician 2021; 24:E539-E554 (32).

Appendix Table 6. *Characteristics of comparative fluoroscopic epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
								Long-Term			
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	> 6 mos.	≥ 12 mos.	24 mos.	
CAUDAL VERSUS INTERLAMINAR											
Ackerman & Ahmad, 2007 (48) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	NA	NA	Effective in all arms	Effective in all arms	NA	NA	Positive mid-term results in a relatively small trial.
Kamble et al, 2016 (50) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	NA	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	NA	NA	All 3 techniques were effective	NA	NA	NA	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.

Appendix Table 6 (cont.). *Characteristics of comparative fluoroscopic epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Pandey, 2016 (51) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	NA	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	NA	*P*	*P*	*P*	NA	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.
CAUDAL VERSUS TRANSFORAMINAL											
Ackerman & Ahmad, 2007 (48) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	NA	NA	Effective in all arms	Effective in all arms	NA	NA	Positive mid-term results in a relatively small trial.

Appendix Table 6 (cont.). *Characteristics of comparative fluoroscopic epidural injections in lumbar disc herniation.*

Study **Study Characteristics** **Methodological Quality Scoring**	**Participants and Interventions**	**Outcome Measures**	**Pain Relief and Function**				**Results**				**Comment(s)**
								Long-Term			
			3 mos.	**6 mos.**	**12 mos.**	**24 mos.**	**Short-term ≤ 6 mos.**	**> 6 mos.**	**≥ 12 mos.**	**24 mos.**	
Kamble et al, 2016 (50) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	NA	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	NA	NA	All 3 techniques were effective	NA	NA	NA	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.
Pandey, 2016 (51) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	NA	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	NA	*P*	*P*	*P*	NA	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.

Appendix Table 6 (cont.). *Characteristics of comparative fluoroscopic epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Singh et al, 2017 (52) RA, AC, F Single level prolapsed lumbar intervertebral disc Quality Scores: Cochrane = 8/13 IPM-QRB = 30/48	Number of patients = 80 Caudal with steroids group = 40 2 mL of methylprednisolone, 80 mg along with lignocaine 2% diluted in 20 mL of normal saline 3 caudal epidural injections were given at an interval of 3 weeks irrespective of previous epidural injection effect SNRB = 40 A single injection of 2 mL of methylprednisolone, 80 mg, mixed with 5 mL of lignocaine 2%	VAS, ODI & significant pain relief of 50%	VAS Caudal vs. SNRB = 61.5% vs. 55.5% ODI decreased caudal vs. SNRB = 64.6% vs. 52.8%	VAS Caudal vs. SNRB= 59.6% vs. 52.9% ODI decreased caudal vs. SNRB = 65.1% vs. 48.6%	VAS Caudal vs. SNRB= 58.2% vs. 46.8% ODI decreased caudal vs. SNRB = 65.4% vs. 46.7%	NA	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Caudal epidural superior to SNRB with steroids	Positive short-term and long-term relief in both caudal and SNRB; however, relief in the caudal group was superior. However, this study suffered with multiple limitations of 3 caudal epidural injections compared to one SNRB and high volumes of injections, which are clinically inappropriate in both caudal and SNRB groups.
INTERLAMINAR VERSUS TRANSFORAMINAL											
Ackerman & Ahmad, 2007 (48) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 8/13 IPM-QRB = 25/48	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal = 30 Methylprednisolone + saline Number of injections = 1 to 3	Numeric pain score (0 - 10), rating of pain relief, ODI, BDI, contrast dispersion pattern Follow-up: 24 weeks	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	NA	NA	Effective in all arms	Effective in all arms	NA	NA	Positive mid-term results in a relatively small trial.

Appendix Table 6 (cont.). *Characteristics of comparative fluoroscopic epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
								Long-Term			
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	> 6 mos.	≥ 12 mos.	24 mos.	
Kamble et al, 2016 (50) RA, AC, F Single level disc prolapse Quality Scores: Cochrane = 9/13 IPM-QRB = 32/48	Transforaminal = 30 Number of injections = 1-3 Interlaminar = 30 Number of injections = 1-3 Caudal = 30 Number of injections = 1-3	VAS, ODI	NA	Transforaminal = VAS baseline 7.1 ± 0.7 to 2.6 ± 0.7 ODI = 37.7 ± 2.83 to 16.8 ± 2.53 Interlaminar = VAS baseline 7.0 ± 0.7 to 3.4 ± 1.4 ODI = 36.9 ± 2.82 to 21.4 ± 6.08 Caudal = VAS baseline 7.2 ± 0.6 to 3.5 ± 1.0. ODI = 38.3 ± 2.78 to 21.9 ± 3.35	NA	NA	All 3 techniques were effective	NA	NA	NA	While all 3 techniques were effective, transforaminal group showed superiority. However, there was no difference between caudal and interlaminar approaches.
Pandey, 2016 (51) RA, AC, F Disc prolapse Quality Scores: Cochrane = 8/13 IPM-QRB = 29/48	Total = 140 patients Caudal = 82 Transforaminal = 40 Interlaminar = 18 All were treated with steroid and local anesthetic with or without sodium chloride solution	JOA score	NA	JOA scores Caudal = baseline 15.39 to 24.30 Transforaminal = baseline 15.57 to 26.65 Interlaminar = baseline 15.33 to 25	JOA scores Caudal = baseline 15.39 to 24.02 Effectiveness = 74.3% Transforaminal = baseline 15.57 to 26.55 Effectiveness = 90% Interlaminar = baseline 15.33 to 24.72 Effectiveness = 77.7%	NA	*P*	*P*	*P*	NA	In comparing caudal epidural with interlaminar and transforaminal, authors showed response in 74.3% with caudal route, 77.7% with interlaminar, and 90% with transforaminal approach. Overall results are positive. There is no significant difference between caudal and interlaminar; however, transforaminal appears to be superior.

Appendix Table 6 (cont.). *Characteristics of comparative fluoroscopic epidural injections in lumbar disc herniation.*

Study Study Characteristics Methodological Quality Scoring	Participants and Interventions	Outcome Measures	Pain Relief and Function				Results				Comment(s)
			3 mos.	6 mos.	12 mos.	24 mos.	Short-term ≤ 6 mos.	Long-Term > 6 mos.	Long-Term ≥ 12 mos.	Long-Term 24 mos.	
Rados et al, 2011 (53) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 9/13 IPM-QRB = 30/48	Total = 64 IL = 32 TF = 32 Lidocaine with methylprednisolone Number of injections = 1 to 3	VAS, ODI, 50% pain relief Follow-up: 6 months	NA	Interlaminar lidocaine with methylprednisolone = 53% Transforaminal lidocaine with methylprednisolone = 63%	NA	NA	Effective with both approaches	NA	NA	NA	• Positive results with short follow-up period in comparison of 2 approaches with lidocaine with methylprednisolone
Ghai et al, 2014 (54) RA, AC, F Disc herniation or radiculopathy Quality Scores: Cochrane = 10/13 IPM-QRB = 42/48	Total = 62 Parasagittal interlaminar = 32 Transforaminal = 30 2 mL of methylprednisolone (80 mg) mixed with 2 mL of normal saline for both PIL and transforaminal groups Number of epidural steroid injections: Transforaminal group: 60 PIL group: 58 Average procedures: 2	Visual analog scale, Oswestry Disability questionnaire, significant improvement, greater than 50% pain relief from baseline, Patient Global Impression	PIL group: 78% Transforaminal group: 77%	PIL group: 75% Transforaminal group: 77%	PIL group: 69% Transforaminal group: 77%	NA	Effectiveness in both arms	Effectiveness in both arms	Effectiveness in both arms	NA	This is relatively small active control trial with a long-term follow-up assessing the role of parasagittal interlaminar epidural injections and transforaminal epidural injections showing equal improvement with steroids without local anesthetic.

RA = Randomized; AC = Active Control; F = Fluoroscopy; IPM-QRB = Interventional Pain Management techniques - Quality Appraisal of Reliability and Risk of Bias Assessment; ODI = Oswestry Disability Index; BDI = Beck Depression Inventory; VAS = Visual Analog Scale; JOA – Japanese Orthopaedic Association; NA = Not Applicable; P = Positive; SNRB – selective nerve root block; PIL = Parasagittal Interlaminar

Adapted from: Manchikanti L, et al. Epidural injections for lumbar radiculopathy or sciatica: A comparative systematic review and meta-analysis of Cochrane review. Pain Physician 2021; 24:E539-E554 (32).