Systematic Review

Epidural Injections for Lumbar Radiculopathy or Sciatica: A Comparative Systematic Review and Meta-Analysis of Cochrane Review

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Background: Epidural injections are one of the commonly performed procedures in managing low back and lower extremity pain. In the past, Pinto et al and Chou et al performed systematic reviews and meta-analyses with a recent update from Oliveira et al showing lack of effectiveness of epidural steroid injections in managing lumbar radiculopathy. In contrast, multiple other systematic reviews and meta-analyses have supported the efficacy and use of epidural injections utilizing fluoroscopic guidance.

Study Design: A systematic review and meta-analysis of randomized controlled trials (RCTs) of epidural injections in managing chronic low back and lower extremity pain with sciatica or lumbar radiculopathy.

Objectives: To assess the efficacy of 3 categories of epidural injections for lumbar radiculopathy or sciatica performed utilizing saline with steroids, local anesthetic alone, or steroids with local anesthetic.

Methods: In this systematic review and meta-analysis, RCTs with a placebo control or an active control design, performed under fluoroscopic guidance, with at least 6 months of follow-up were 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.
Literature search was performed through January 2021. Methodological quality assessments were performed. Evidence was summarized utilizing principles of best evidence synthesis.

Results: In this analysis, a total of 21 RCTs were utilized with at least 6 months of follow-up and performed under fluoroscopic guidance. However, only 6 of 25 trials from Cochrane review met inclusion criteria for this review. Based on qualitative analysis, of the 21 trials included in the present analysis, there was only one placebo-controlled trial found to be negative.
With conventional meta-analysis, there was no significant difference among the studies because all of the studies were active control with local anesthetic or local anesthetic and steroids. Further, with single-arm analysis, of the 5 trials included in that portion of the study, significant improvement was seen with local anesthetic alone compared to local anesthetic and steroids. There was a tendency for better improvement with steroids in terms of both pain relief and functional status.
The level of evidence is Level I or strong for local anesthetic with steroids and Level I to II or moderate to strong for local anesthetic as a single agent based on multiple relevant high quality RCTs.

Limitations: Despite multiple trials available, there is a paucity of true RCTs performed under fluoroscopic guidance with any of the approaches.

Conclusion: Epidural injections with or without steroids for radiculopathy showed significant effectiveness with Level I or strong evidence for local anesthetic with steroids and Level II to I or moderate to strong evidence with local anesthetic alone.

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

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Epidural injections are among the commonly performed procedures in managing pain secondary to disc herniation and radiculopathy with evidence demonstrated by multiple systematic reviews of controlled studies and evidence-based guidelines (1-15). The studies of utilization of patterns showed increases initially followed by declines in recent years for epidural injections, mirroring utilization of other interventional techniques (16-23). In addition, the study of expenditures of epidural procedures in chronic spinal pain from 2009 to 2019 (18) showed a decrease in total expenditures, costs per procedure, and the number of patients receiving epidural procedures. Despite these factors, discordant conclusions have been reached by Pinto et al (24), Chou et al (25), Bicket et al (26) and a subsequent Cochrane review (27). All of these manuscripts considered local anesthetics as placebos, despite the extensive literature showing otherwise, concluding that these were ineffective as there was no significant differences between both groups without performing single-arm analysis or comparing within the groups (1,4-7,13-15,21,29).

The recent Cochrane systematic review (27), followed by a version published in Spine (28) concluded that a review of 20 placebo-controlled trials provided moderate quality evidence that epidural corticosteroid injections are effective, although the effects are small and short-term. The flaw in this conclusion is that local anesthetics are not innocuous. Their extensive antiinflammatory effects, long-lasting effects beyond pharmacologic profiles, the non-significant difference between steroids and local anesthetic and abundance of experimental and clinical evidence leads, in our opinion, to inaccurate evidence synthesis (1,4-10,13-15,29-32).

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 compare our results with those of the Cochrane review (28) as we did (14) with Chou et al (25) previously.

Methods

The methodology of the present study included utilization of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (www.prisma-statement.org) and the Institute of Medicine (IOM) standards for systematic reviews and comparative effectiveness research (CER) (1,13-15,19,33,34) and other relevant publications. There was no external funding received for the preparation of this manuscript and there are no undisclosed conflicts.

Based on the Cochrane review, this present manuscript focuses on the effectiveness of epidural injections for radiculopathy or sciatica when provided with administration of sodium chloride solution or with local anesthetic in placebo-controlled trials. In this manuscript, we will separate true placebo trials from active-controlled trials. Conventional dual-arm and single-arm analysis will be performed to assess the effect of each modality of treatment with either noninferiority or lack of superiority and assessment of local anesthetics with or without steroids.

In contrast to Oliveira et al (27,28), we defined placebo interventions as the administration of an inert substance into the epidural space, over the nerve root, or in remote tissues. In addition, an active substance such as corticosteroid into soft tissues was also considered as placebo. All local anesthetic injections into the epidural space or over the nerve root were considered to be active controls. In addition, all other RCTs meeting prespecified criteria were included. Consequently, some studies utilized by Oliveira et al (27,28) were excluded if they failed to meet our pre-specified inclusion criteria of fluoroscopic guidance and with a minimum of 6-month follow-up.

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 Oliveira et al's systematic reviews. For the search purposes, we included PubMed from 1966, www.ncbi.nlm.nih.gov/pubmed; Cochrane library, www.thecochranelibrary.com; Embase, www.embase.com; US National Guideline Clearinghouse (NGC), www.guideline.gov/; Google Scholar, https://scholar.google.com; previous systematic reviews and cross references and all other sources including unindexed journals and abstracts through January 2021.

Search Criteria

((((((((((((((((chronic low back pain) OR disc herniation) OR discogenic pain) OR herniated lumbar discs) OR nerve root compression) OR lumbosciatic pain) OR postlaminectomy) OR lumbar surgery syndrome) OR radicular pain) OR radiculitis) OR sciatica) OR spinal fibrosis) OR spinal stenosis) AND ((((((((((epidural injection) OR epidural steroid) OR epidural perineural injection) OR interlaminar epidural) OR intraarticular corticosteroid) OR nerve root blocks) OR periradicular

infiltration) OR transforaminal injection) OR corticosteroid) OR methylprednisolone))) AND ((meta-analysis [pt] OR randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw])) OR (placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp])))))

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. We 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 updated from recent systematic reviews performed for guideline preparation (1).

At least 2 of the review authors independently, in an unblinded standardized manner, acquired the literature, selected the studies, performed the methodological quality assessment, and analyzed the evidence. Any disagreements between reviewers were resolved by a third author and consensus. If there were any conflicts of interest with a manuscript, e.g., authorship, the review authors were recused from assessment and analysis.

The quality assessment of each individual article used in this analysis was performed by comparing the analysis performed by Oliveira et al (27,28) with an independent assessment using Cochrane review criteria (Appendix Table 1) (35) and Interventional Pain Management Techniques - Quality Appraisal of Reliability and Risk of Bias Assessment (IPM-QRB) criteria (Appendix Table 2) (36).

Utilizing Cochrane review criteria (35) or IPM-QRB (36), studies meeting the inclusion criteria with a score of at least 9 of 13 or 32 to 48, respectively, were considered high quality and 4 to 7 or 16 to 31 were considered moderate quality; these were included in the review. Those with a score of less than 4 or 16 were considered low quality.

Data Synthesis and Analysis

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

Dual-Arm Meta-Analysis

For dual-arm meta-analysis, software Review Manager [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

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).

with 95% confidence intervals. Data were plotted using forest plots to evaluate treatment effects. Heterogeneity was interpreted through I^2 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. This is in contrast to Oliveira et al who utilized differences between 2 active-controlled trials and also considered a larger number of studies as placebo even though these studies were active-control (27,28). We believe that in both of the above situations, Oliveira et al made an error in methodology.

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 (2-15,38-44). 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 (2-15,38-44).

Consequently, in this report, we have utilized either ≥ 50% relief from the baseline pain score or a change of at least 3 points on an 11-point pain scale. A ≥ 30% decrease of disability scores was considered clinically significant.

Results

Figure 1 shows the literature search and selection of the manuscripts for inclusion. After full text review and exclusion of duplicates, we identified 21 trials (45-66) meeting inclusion criteria. Of these, a total of 7 studies assessed caudal epidural injections (45,46,55-59), 10 studies assessed interlaminar epidural injections (47-49,55,57,58,60-63), and 12 studies assessed transforaminal epidural injections (50-55,57,58,60,61,64-66).

Of the 25 trials included by Oliveira et al (28), multiple trials did not meet the present predefined inclusion criteria (67-85). Of the 21 included trials in this review (45-66), 15 trials were not included in Oliveira et al's review (28), consequently, only 6 trials were included in both reviews (45,47,48,50,51,54).

Among the included manuscripts, one was a placebo-controlled trial (50), another trial compared epidural steroid injection with conservative management (46), 7 trials (45,47-49,51,52,54) presented comparisons of local anesthetic with steroids, one trial (66) presented a comparison between different types of steroids, and 6 trials (55,57-61) presented comparisons of different techniques.

Methodological Quality Assessment

Appendix Tables 3 and 4 show the scoring for methodological quality assessment of all RCTs utilizing the Cochrane review criteria (35) and IPM-QRB criteria (36).

Table 2 shows the scoring for methodological quality assessment of RCTs of lumbar epidural injections, with a comparison between 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 (65,66).

Effectiveness of Epidural Injections

Descriptive characteristics of included studies are shown in Appendix Tables 3 and 4.

Of the studies included in this assessment, there was one placebo controlled trial (50) (Appendix Tables 5 to 7), and one study which compared conservative management (46), 7 studies compared local anesthetic alone with local anesthetic and steroids (45,47-49,51,52,54), and the remaining studies either compared technical aspects or dose responses as shown in Appendix Table 8.

Evidence Synthesis

Evidence synthesis was performed by qualitative and quantitative analysis.

Qualitative Synthesis

Qualitative synthesis of evidence included all 21 studies (45-66) with only one placebo-controlled trial and a second RCT compared with conservative management (46,50). All other studies were active-controlled trials.

Meta-Analysis

Meta-analysis was performed utilizing conven-

tional and single-arm analysis.

Placebo-Controlled Trials

There was only one placebo-controlled trial (50) and the second one compared epidural steroid injections with conservative management (46). Consequently, we excluded them from 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.

Meta-Analysis Results

Figure 2 shows the change in pain level using the numeric rating scale (NRS) from baseline at 6 months.

There were 5 studies (45,47-49,51) with 527 patients that compared the combination of local anesthetics with steroids vs. local anesthetic in dual-arm meta-analysis. Results showed no statistically significant difference between these two groups [SMD 0.19 (-0.49, 0.87), $P = 0.58$] (Fig. 2A).

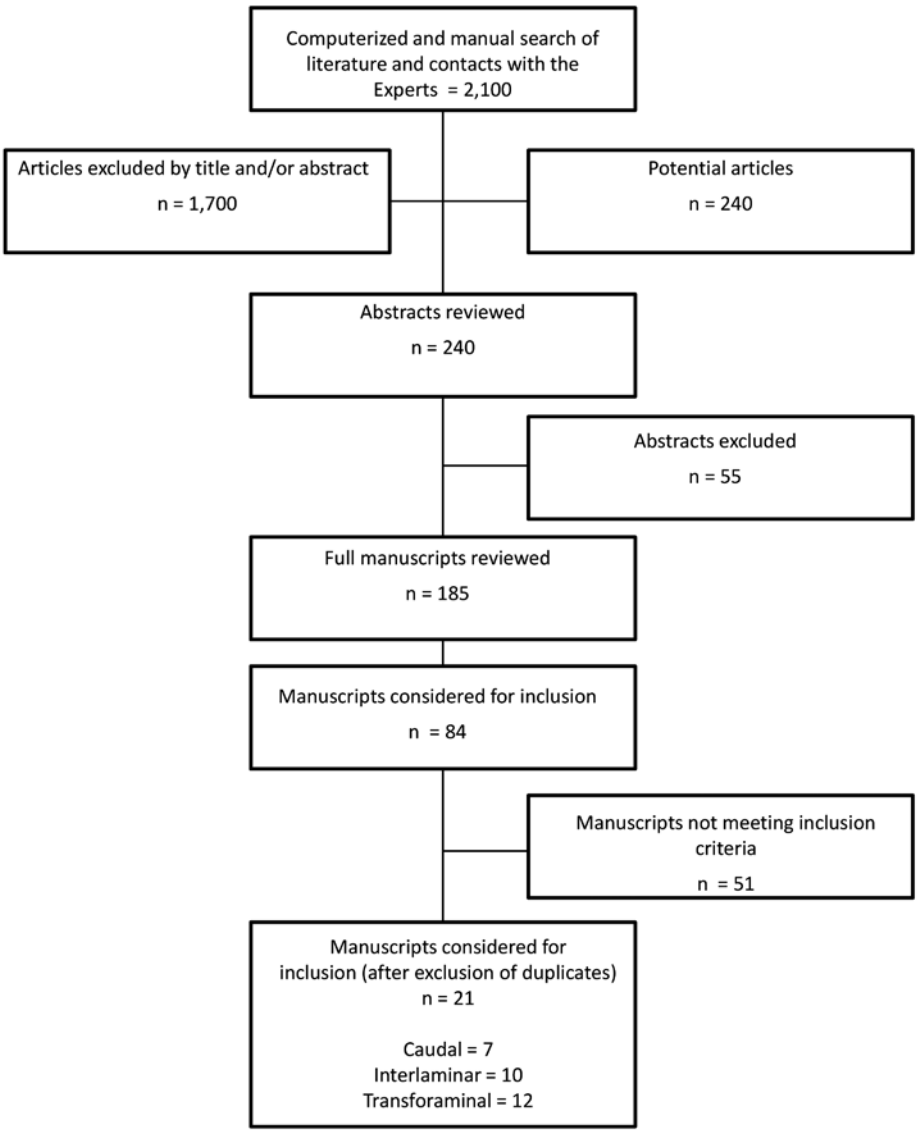

Fig. 1. *PRISMA Flow diagram illustrating published literature evaluating epidural injection therapy in managing disc herniation, radiculopathy, or sciatica.*

Figure 2B shows the results of a single-arm analysis utilizing local anesthetics. Five studies (45,47-49,51) were used to assess pain score after 6 months using NRS in patients who underwent epidural local anesthetic injections. As shown in Fig. 2B, the pooled mean difference of pain score from baseline to 6 months of follow-up was decreased by 3.637 points (95% CI: -3.787 to – 3.487, $P < 0.001$).

Figure 2C shows results of a single-arm analysis utilizing a combination of epidural steroids and local anesthetics. Five studies (45,47-49,51) were used to assess pain score after 6 months using NRS in patients who underwent epidural steroid injections. As shown in Fig. 2C, the pooled mean difference of pain score from baseline to 6 months of follow-up was decreased by 4.105 points (95% CI: -4.2024 to – 4.005, $P < 0.001$).

Based on conventional dual-arm analysis, even though there is no significant difference between local

Table 2. *Methodological quality assessment of epidural injections with caudal, interlaminar, and transforaminal approaches in managing pain of lumbar radiculopathy or sciatica.*

Trial	Cochrane Criteria	IPM-QRB Criteria	Quality Grading (high, moderate, low) Cochrane/IPM-QRB
Manchikanti et al (45)	12/13	44/48	High
Ackerman & Ahmad (55)	8/13	25/48	Moderate
Dashfield et al (56)	10/13	33/48	High
Murakibhavi & Khemka (46)	8/13	27/48	Moderate
Kamble et al (57)	9/13	32/48	High
Pandey (58)	8/13	29/48	Moderate
Singh et al (59)	8/13	30/48	Moderate
Manchikanti et al (47)	11/13	44/48	High
Ghai et al (48)	10/13	39/48	High
Ökmen & Ökmen 2017 (49)	12/13	40/48	High
Rados et al (60)	9/13	30/48	High
Ghai et al (61)	10/13	42/48	High
Candido et al (62)	10/13	37/48	High
Amr (63)	12/13	38/48	High
Karppinen et al (50)	13/13	34/48	High
Manchikanti et al (51)	11/13	44/48	High
Riew et al (52,53)	9/13	32/48	High
Tafazal et al (54)	11/13	32/48	High
Vad et al (64)	5/13	16/48	Moderate
Jeong et al (65)	10/13	31/48	High / Moderate
Kennedy et al (66)	10/13	30/48	High / Moderate

anesthetic and local anesthetic and steroids, there is a slight advantage for local anesthetic with steroids. Following the results in single-arm analysis as shown in Fig. 2B with local anesthetic, the improvement was seen by a 3.637 point decrease, whereas with local anesthetic with steroids, as shown in Fig. 2C, the improvement was a decrease of 4.105 points. Even though there is no significant difference between the groups, there is a tendency towards improved results for local anesthetic with steroids.

Figure 3 shows the change in functionality level using Oswestry Disability Index (ODI) from baseline at 6 months.

There were 5 studies (45,47-49,51) with 527 patients that compared local anesthetics with the combination of local anesthetics and steroids. Analysis showed no statistically significant difference between these two groups [SMD 0.70 (-0.11, 1.51), $P = 0.09$] (Fig. 3A).

Figure 3B shows results of a single-arm analysis utilizing local anesthetics. Five studies (45,47-49,51) were used to assess a functionality score after 6 months using ODI in patients who underwent epidural local anesthetic injections. As shown in Fig. 3B, the pooled mean difference of pain score from baseline to 6 months of follow-up was decreased by 13.697 points (95% CI: -13.785 to -13.609, $P < 0.001$).

Fig. 3C shows the results of a single-arm analysis utilizing a combination of epidural steroids and local anesthetics. Five studies (45,47-49,51) were used to assess a functionality score after 6 months using ODI in patients who underwent epidural steroid injections. As shown in Fig. 3C, the pooled mean difference of pain score from baseline to 6 months of follow-up was a decrease of 16.258 points (95% CI: -16.744 to -15.772, $P < 0.001$).

Similar to pain relief analysis, functionality analysis shows statistically similar results in patients receiving local anesthetic alone compared to local anesthetic with steroids. However, there was a trend towards greater improvement in patients with local anesthetic and steroids. Single-arm analysis with local anesthetic alone showed an improvement of functionality with a decrease of 13.697 points as shown in Fig. 3B, compared to local anesthetic and steroids a decrease of 16.258 points as shown in Fig. 3C. Thus, once again, there is a tendency towards local anesthetic with steroids being superior, concurring with the results of pain relief.

Figure 4 shows the change in pain level using NRS from baseline at 12 months.

There were 5 studies (45,47-49,51) with 527 patients that compared local anesthetics with local anesthetics and steroids which showed no statistically significant difference between these two groups [SMD 0.07 (-0.56, 0.69), $P = 0.84$] (Fig. 4A).

Figure 4B shows the results of a single-arm analysis utilizing a local anesthetic. Five studies (45,47-49,51) were used to assess pain score after 12 months using NRS in patients who underwent epidural local anesthetic injections. As shown as in Fig. 4B, the pooled mean difference of pain score from baseline to 12 months of follow-up was a decrease of 3.773 points (95% CI: -3.887 to – 3.660, $P < 0.001$).

Figure 4C shows results of a single-arm analysis

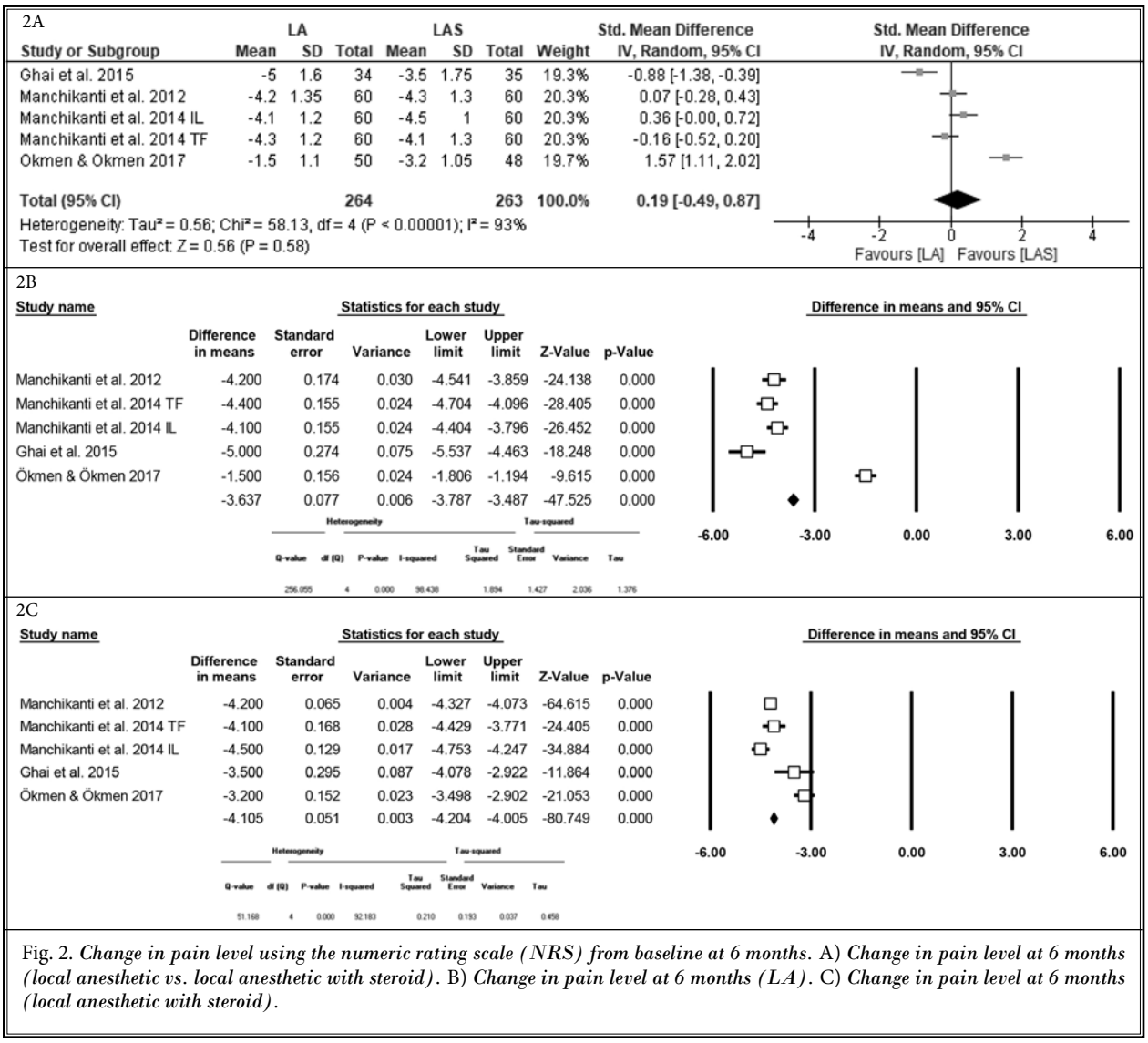

Fig. 2. *Change in pain level using the numeric rating scale (NRS) from baseline at 6 months.* A) *Change in pain level at 6 months (local anesthetic vs. local anesthetic with steroid).* B) *Change in pain level at 6 months (LA).* C) *Change in pain level at 6 months (local anesthetic with steroid).*

utilizing a combination of local anesthetic and steroids. Five studies (45,47-49,51) were used to assess pain score after 6 months using NRS in patients who underwent epidural steroid injections. As shown as in Fig. 4C, the pooled mean difference of pain score from baseline to 12 months of follow-up was decreased by 4.388 points (95% CI: -4.483 to – 4.294, $P < 0.001$).

At one-year follow-up with conventional dual-arm analysis, the results were with no significant difference between local anesthetic alone compared to local anesthetic with steroids (Fig. 4A). In this analysis, there was no tendency for either treatment to be superior. With single-arm analysis, as shown in Fig. 4B, with local anesthetic alone, the difference of pain scores from baseline to 12 months of follow-up was a 3.773 point decrease compared to local anesthetic with steroids as shown in Fig. 4C with a decline of 4.388 points with a tendency towards superior relief with local anesthetic combined with steroids.

Figure 5 shows the change in functionality level using ODI from baseline at 12 months.

There were 5 studies (45,47-49,51) with 527 patients that compared the combination of local anesthetics with steroids vs. local anesthetic that showed no statistically significant difference between these two groups [SMD 0.61 (-0.14, 1.35), $P = 0.11$] (Fig. 5A).

Figure 5B shows results of a single-arm analysis utilizing local anesthetics. Five studies (45,47-49,51)

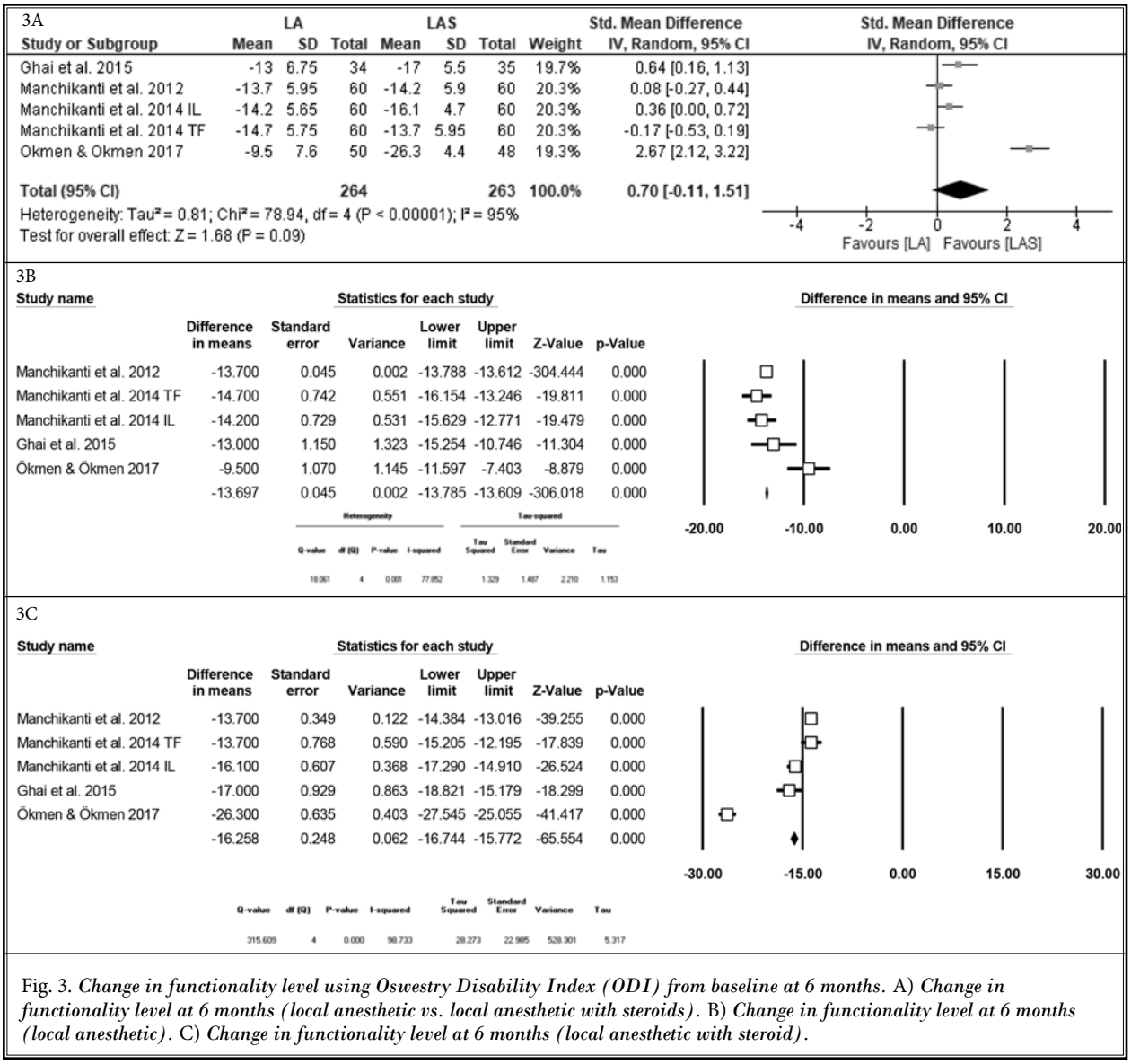

Fig. 3. *Change in functionality level using Oswestry Disability Index (ODI) from baseline at 6 months.* A) *Change in functionality level at 6 months (local anesthetic vs. local anesthetic with steroids).* B) *Change in functionality level at 6 months (local anesthetic).* C) *Change in functionality level at 6 months (local anesthetic with steroid).*

were used to assess a functionality score after 12 months using ODI in patients who underwent epidural local anesthetic injections. As shown as in Fig. 5B, the pooled mean difference of pain score from baseline to 12 months of follow-up was a decrease of 11.809 points (95% CI: -11.993 to -11.624, $P < 0.001$).

Figure 5C shows results of a single-arm analysis utilizing epidural steroids and local anesthetics. Five studies (45,47-49,51) were used to assess a functionality score after 12 months using ODI in patients who underwent epidural steroid injections. As shown in Fig. 5C, the pooled mean difference of pain score from baseline to 6 months of follow-up was a decrease of 14.988 points (95% CI: -15.161 to -14.814, $P < 0.001$).

As shown in Fig. 5A with conventional dual-arm analysis, there was no significant difference between local anesthetic alone compared to local anesthetic with steroids. However, there was tendency towards better improvement with local anesthetic and steroids. In addition, with single-arm analysis as shown in Fig. 5B, with functionality at 12-month follow-up with local anesthetic alone, the improvement was an 11.809 point decrease of disability scores compared to the local anesthetic and steroids group as shown in Fig. 5C with a

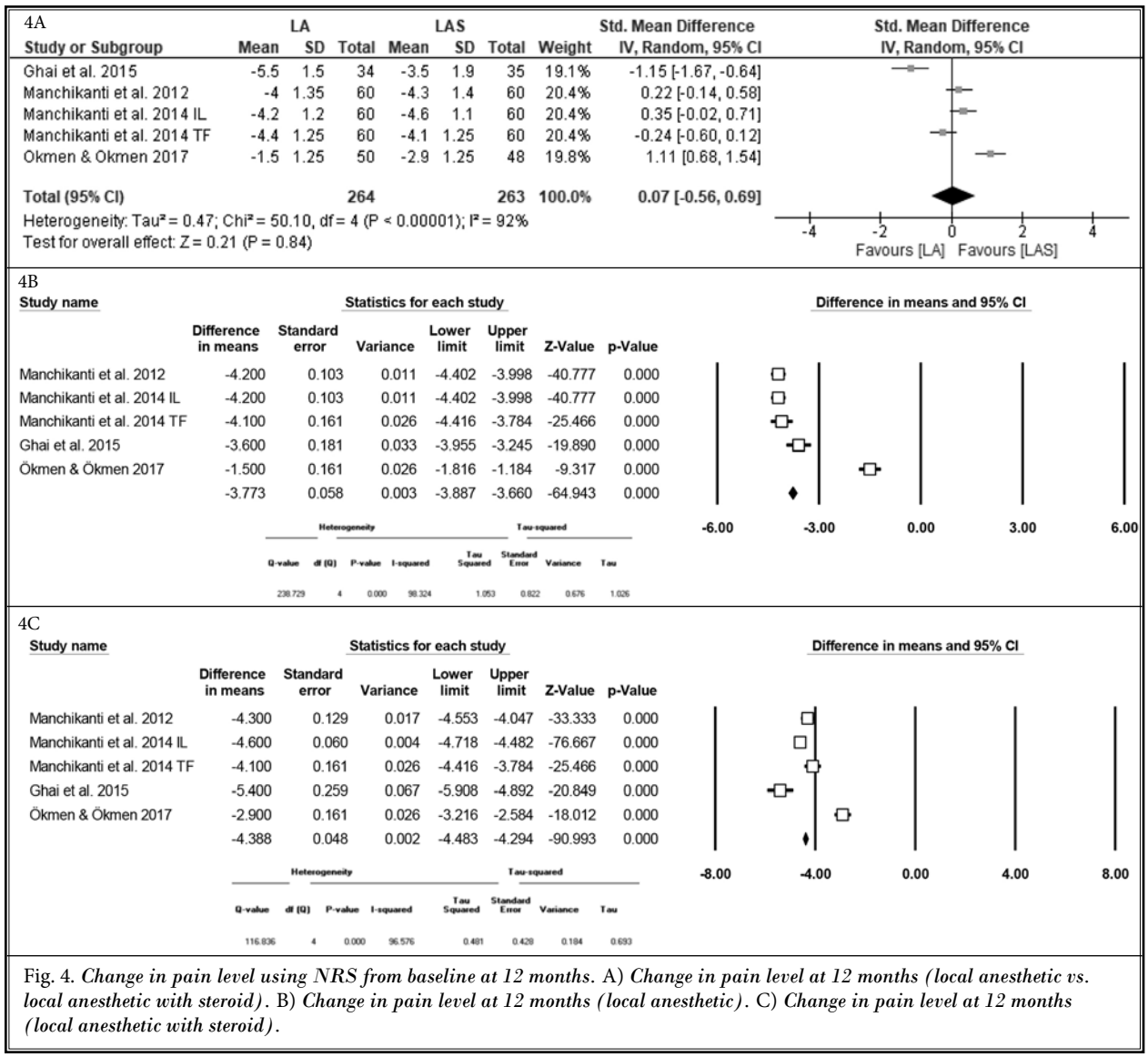

Fig. 4. *Change in pain level using NRS from baseline at 12 months.* A) *Change in pain level at 12 months (local anesthetic vs. local anesthetic with steroid).* B) *Change in pain level at 12 months (local anesthetic).* C) *Change in pain level at 12 months (local anesthetic with steroid).*

decrease of 14.988. Consequently, it shows a tendency towards better improvement with local anesthetic and steroids compared to local anesthetic alone.

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.

Figures 3-5 showed the results of meta-analysis of epidural steroid injections which showed Level I evidence for short-term and long-term improvement for epidural steroid injections. This was confirmed with appropriate evidence analysis utilizing a single-arm analysis for comparative studies, as well as all the studies with available data based on the data. Dual-arm analysis and single-arm analysis for a limited number of studies showed significant improvement.

Discussion

The Cochrane review converted active-controlled into placebo-controlled trials, resulting in conclusions that we believe are not based in proper interpretation of the evidence. The present systematic review and meta-analysis shows Level I evidence for caudal, inter-

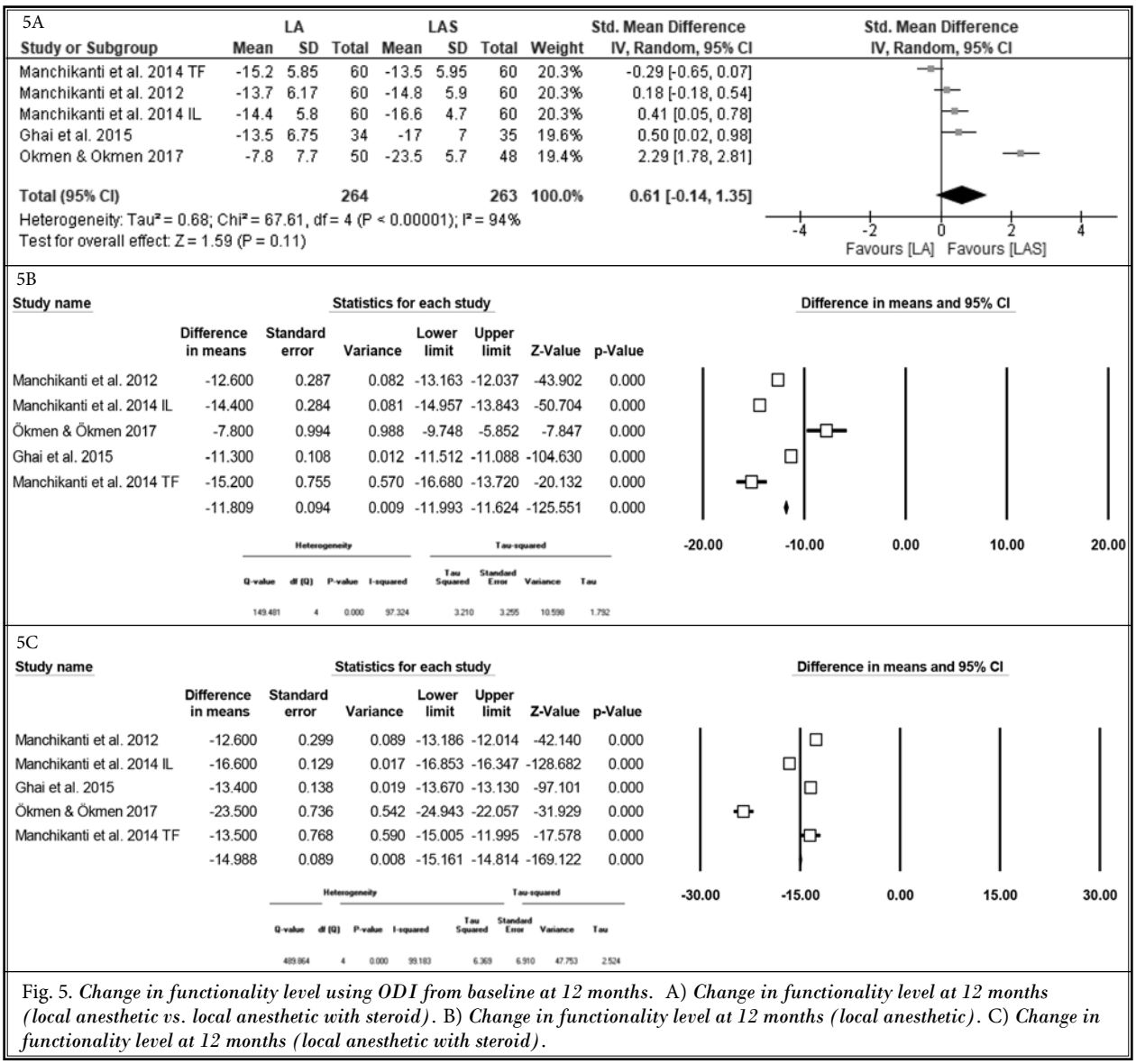

Fig. 5. *Change in functionality level using ODI from baseline at 12 months.* A) *Change in functionality level at 12 months (local anesthetic vs. local anesthetic with steroid).* B) *Change in functionality level at 12 months (local anesthetic).* C) *Change in functionality level at 12 months (local anesthetic with steroid).*

laminar, and transforaminal epidural injections in managing lumbar radiculopathy or sciatica with local anesthetic with steroids or local anesthetic alone. Based on qualitative and quantitative analysis, which included conventional single-arm and dual-arm meta-analysis, based on the 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. 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; however, for quantitative analysis, only 5 studies were included with a total of 527 patients which compared the combination of local anesthetics with steroids versus local anesthetic alone in dual-arm meta-analysis (45,47-49,51). Similarly, for single-arm analysis, these studies were also utilized for short-term and long-term follow-up showing positive results. 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.

Based on the qualitative synthesis of evidence of one placebo-controlled trial (50), transforaminal epidural steroid injections with bupivacaine, with saline showed a lack of effectiveness. Karpinnen et al (50) performed this trial in 2001 with 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 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. In a subgroup analysis (86), they adjusted between group treatment differences at each follow-up assessment with number of patients free of leg pain with a cut-off of 75% improvement, and efficacy by the area-under-the-curve method. For the cost effectiveness estimate, the total costs were divided by the number of responders. The results showed that in cases of 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, steroid seemed to have prevented operations for contained herniations, costing $12,666 less per responder in the steroid group. For extrusions, steroid seemed to increase the operation rate, and the steroid infiltration was more expensive, costing $4,445 per responder. We believe that the primary study suffered from inappropriate placebo design and based on the author's comments in the 2001 Spine paper consider this to be a positive study.

The second RCT (46) compared caudal epidural with local anesthetic and methylprednisolone to conservative management. Murakibhavi and Khemka in 2011 assessed 50 patients with controlled conservative management and an additional 52 patients with caudal epidural utilizing 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 were 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, comparison of preganglionic and postganglionic approaches, and 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 (50,86) were controversial. Among the other 11 trials, 6 (51,52,54,58,61,64) showed long-term follow-up with positive results at one-year follow-up. The remaining trials were of shorter duration; however, they also showed positive short-term results. Of these, 2 trials (51,54) compared lidocaine with steroids and one study bupivacaine alone or bupivacaine with steroids was compared (52). 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 alone and also avoided surgery in 71% of the steroid group compared to 33% of bupivacaine group.

There was one controlled trial comparing conservative management to local anesthetic and steroid treatment (46), 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 (45) with comparative analysis of lidocaine alone or lidocaine with steroids and showed at the end of the one-year a 67% positive response with local anesthetic and 72% positive 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. Other studies compared caudal, interlaminar, versus transforaminal or caudal with transforaminal with improvement seen in all groups. Further, in one study (56), the 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 (45) 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.

Our results are in concordance with guidelines and multiple other systematic reviews (1,2,4-15). A systematic review by Manchikanti et al (5) evaluated if epidural injection of sodium chloride solution was a true placebo using conventional dual-arm and a single-arm analysis. Eight trials met 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 analysis, 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.

In another systematic review and meta-analysis, Manchikanti et al (6) 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 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 with the conclusion that local anesthetics are ineffective leads to inappropriate conclusions.

Knezevic et al (7), 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 demonstrated that utilizing single-arm analysis, clear effect on each modality was demonstrated with lidocaine, as well as lidocaine with steroids. Therefore, once again, it was shown that it is inappropriate to judge that lidocaine is a placebo.

Lee et al (10), 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 steroid. Mesregah et al (85) 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), 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 addition of steroids.

Discordant conclusions (24-28) may thus be 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 (33,34) 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 for a variety of role groups (13,33,34,87-93). In addition, along on the same lines, Cappola and FitzGerald (94) from the Institute for Transitional Medicine and Therapeutics have 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.

Conclusion

This systematic review with the assessment of 21 RCTs, with at least 6 month follow-up and performed under fluoroscopic guidance, with assessment of methodologic quality, qualitative and quantitative evidence synthesis showed Level I or strong evidence for the effectiveness of lumbar epidural injections with local anesthetic and steroids and Level II to I or moderate to strong evidence for local anesthetic alone in managing lumbar radiculopathy or sciatica secondary to lumbar disc herniation.

Author Contributions

The study was designed by LM, NK, AA, and JH, 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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Appendix Table 1. *Sources of risk of bias and Cochrane Review rating system.*

Bias Domain	**Source of Bias**		**Possible Answers**
Selection	(1) Was the method of randomization adequate?	A random (unpredictable) assignment sequence. Examples of adequate methods are coin toss (for studies with 2 groups), rolling a dice (for studies with 2 or more groups), drawing of balls of different colors, drawing of ballots with the study group labels from a dark bag, computer-generated random sequence, preordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and preordered list of treatment assignments.	Yes/No/ Unsure
		Examples of inadequate methods are: alternation, birth date, social insurance/security number, date in which they are invited to participate in the study, and hospital registration number.	
Selection	(2) Was the treatment allocation concealed?	Assignment generated by an independent person not responsible for determining the eligibility of the patients. This person has no information about the persons included in the trial and has no influence on the assignment sequence or on the decision about eligibility of the patient.	Yes/No/ Unsure
Performance	(3) Was the patient blinded to the intervention?	Index and control groups are indistinguishable for the patients or if the success of blinding was tested among the patients and it was successful.	Yes/No/ Unsure
Performance	(4) Was the care provider blinded to the intervention?	Index and control groups are indistinguishable for the care providers or if the success of blinding was tested among the care providers and it was successful.	Yes/No/ Unsure
Detection	(5) Was the outcome assessor blinded to the intervention?	Adequacy of blinding should be assessed for each primary outcome separately. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or:	Yes/No/ Unsure
		• for patient-reported outcomes in which the patient is the outcome assessor (e.g., pain, disability): the blinding procedure is adequate for outcome assessors if participant blinding is scored "yes"	
		• for outcome criteria assessed during scheduled visit and that supposes a contact between participants and outcome assessors (e.g., clinical examination): the blinding procedure is adequate if patients are blinded, and the treatment or adverse effects of the treatment cannot be noticed during clinical examination	
		• for outcome criteria that do not suppose a contact with participants (e.g., radiography, magnetic resonance imaging): the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed when assessing the main outcome	
		• for outcome criteria that are clinical or therapeutic events that will be determined by the interaction between patients and care providers (e.g., cointerventions, hospitalization length, treatment failure), in which the care provider is the outcome assessor: the blinding procedure is adequate for outcome assessors if item "4" (caregivers) is scored "yes"	
		• for outcome criteria that are assessed from data of the medical forms: the blinding procedure is adequate if the treatment or adverse effects of the treatment cannot be noticed on the extracted data	
Attrition	(6) Was the drop-out rate described and acceptable?	The number of participants who were included in the study but did not complete the observation period or were not included in the analysis must be described and reasons given. If the percentage of withdrawals and drop-outs does not exceed 20% for short-term follow-up and 30% for long-term follow-up and does not lead to substantial bias a "yes" is scored. (N.B. these percentages are arbitrary, not supported by literature).	Yes/No/ Unsure
Attrition	(7) Were all randomized participants analyzed in the group to which they were allocated?	All randomized patients are reported/analyzed in the group they were allocated to by randomization for the most important moments of effect measurement (minus missing values) irrespective of noncompliance and cointerventions.	Yes/No/ Unsure

Appendix Table 1 *continued. Sources of risk of bias and Cochrane Review rating system.*

Bias Domain	**Source of Bias**		**Possible Answers**
Reporting	(8) Are reports of the study free of suggestion of selective outcome reporting?	All the results from all prespecified outcomes have been adequately reported in the published report of the trial. This information is either obtained by comparing the protocol and the report, or in the absence of the protocol, assessing that the published report includes enough information to make this judgment.	Yes/No/ Unsure
Selection	(9) Were the groups similar at baseline regarding the most important prognostic indicators?	Groups have to be similar at baseline regarding demographic factors, duration and severity of complaints, percentage of patients with neurological symptoms, and value of main outcome measure(s).	Yes/No/ Unsure
Performance	(10) Were cointerventions avoided or similar?	If there were no cointerventions or they were similar between the index and control groups.	Yes/No/ Unsure
Performance	(11) Was the compliance acceptable in all groups?	The reviewer determines if the compliance with the interventions is acceptable, based on the reported intensity, duration, number and frequency of sessions for both the index intervention and control intervention(s). For example, physiotherapy treatment is usually administered for several sessions; therefore it is necessary to assess how many sessions each patient attended. For single-session interventions (e.g., surgery), this item is irrelevant.	Yes/No/ Unsure
Detection	(12) Was the timing of the outcome assessment similar in all groups?	Timing of outcome assessment should be identical for all intervention groups and for all primary outcome measures.	Yes/No/ Unsure
Other	(13) Are other sources of potential bias unlikely?	Other types of biases. For example: • When the outcome measures were not valid. There should be evidence from a previous or present scientific study that the primary outcome can be considered valid in the context of the present. • Industry-sponsored trials. The conflict of interest (COI) statement should explicitly state that the researchers have had full possession of the trial process from planning to reporting without funders with potential COI having any possibility to interfere in the process. If, for example, the statistical analyses have been done by a funder with a potential COI, usually "unsure" is scored.	Yes/No/ Unsure

Source: Furlan AD, 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 (35).

Appendix Table 2. *Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM – QRB.*

		Scoring
I.	TRIAL DESIGN AND GUIDANCE REPORTING	
1.	CONSORT or SPIRIT	
	Trial designed and reported without any guidance	0
	Trial designed and reported utilizing minimum criteria other than CONSORT or SPIRIT criteria or trial was conducted prior to 2005	1
	Trial implies it was based on CONSORT or SPIRIT without clear description with moderately significant criteria for randomized trials or the trial was conducted before 2005	2
	Explicit use of CONSORT or SPIRIT with identification of criteria or trial conducted with high level reporting and criteria or conducted before 2005	3
II.	DESIGN FACTORS	
2.	Type and Design of Trial	
	Poorly designed control group (quasi selection, convenient sampling)	0
	Proper active-control or sham procedure with injection of active agent	2
	Proper placebo control (no active solutions into active structures)	3
3.	Setting/Physician	
	General setting with no specialty affiliation and general physician	0
	Specialty of anesthesia/PMR/neurology/radiology/ortho, etc.	1
	Interventional pain management with interventional pain management physician	2
4.	Imaging	
	Blind procedures	0
	Ultrasound	1
	CT	2
	Fluoro	3
5.	Sample Size	
	Less than 50 participants in the study without appropriate sample size determination	0
	Sample size calculation with less than 25 patients in each group	1
	Appropriate sample size calculation with at least 25 patients in each group	2
	Appropriate sample size calculation with 50 patients in each group	3
6.	Statistical Methodology	
	None or inappropriate	0
	Appropriate	1
III.	PATIENT FACTORS	
7.	Inclusiveness of Population	
7a.	For epidural procedures:	
	Poorly identified mixed population	0
	Clearly identified mixed population	1
	Disorders specific trials (i.e. well defined spinal stenosis and disc herniation, disorder specific, disc herniation or spinal stenosis or post-surgery syndrome)	2
7b.	For facet or sacroiliac joint interventions:	
	No diagnostic blocks	0
	Selection with single diagnostic blocks	1
	Selection with placebo or dual diagnostic blocks	2
8.	Duration of Pain	
	Less than 3 months	0
	3 to 6 months	1
	> 6 months	2
9.	Previous Treatments Conservative management including drug therapy, exercise therapy, physical therapy, etc.	

Appendix Table 2 con't. *Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM – QRB.*

		Scoring
	Were not utilized	0
	Were utilized sporadically in some patients	1
	Were utilized in all patients	2
10.	Duration of Follow-up with Appropriate Interventions	
	Less than 3 months or 12 weeks for epidural or facet joint procedures, etc. and 6 months for intradiscal procedures and implantables	0
	3 to 6 months for epidural or facet joint procedures, etc., or 1 year for intradiscal procedures or implantables	1
	6 months to 17 months for epidurals or facet joint procedures, etc., and 2 years or longer for discal procedures and implantables	2
	18 months or longer for epidurals and facet joint procedures, etc., or 5 years or longer for discal procedures and implantables	3
IV.	OUTCOMES	
11.	Outcomes Assessment Criteria for Significant Improvement	
	No descriptions of outcomes OR < 20% change in pain rating or functional status	0
	Pain rating with a decrease of 2 or more points or more than 20% reduction OR functional status improvement of more than 20%	1
	Pain rating with decrease of ≥ 2 points AND ≥ 20% change or functional status improvement of ≥ 20%	2
	Pain rating with a decrease of 3 or more points or more than 50% reduction OR functional status improvement with a 50% or 40% reduction in disability score	2
	Significant improvement with pain and function ≥ 50% or 3 points and 40% reduction in disability scores	4
12.	Analysis of all Randomized Participants in the Groups	
	Not performed	0
	Performed without intent-to-treat analysis without inclusion of all randomized participants	1
	All participants included with or without intent-to-treat analysis	2
13.	Description of Drop Out Rate	
	No description of dropouts, despite reporting of incomplete data or ≥ 20% withdrawal	0
	Less than 20% withdrawal in one year in any group	1
	Less than 30% withdrawal at 2 years in any group	2
14.	Similarity of Groups at Baseline for Important Prognostic Indicators	
	Groups dissimilar with significant influence on outcomes with or without appropriate randomization and allocation	0
	Groups dissimilar without influence on outcomes despite appropriate randomization and allocation	1
	Groups similar with appropriate randomization and allocation	2
15.	Role of Co-Interventions	
	Co-interventions were provided but were not similar in the majority of participants	0
	No co-interventions or similar co-interventions were provided in the majority of the participants	1
V.	RANDOMIZATION	
16.	Method of Randomization	
	Quasi randomized or poorly randomized or not described	0
	Adequate randomization (coin toss, drawing of balls of different colors, drawing of ballots)	1
	High quality randomization (Computer generated random sequence, pre-ordered sealed envelopes, sequentially ordered vials, telephone call, pre-ordered list of treatment assignments, etc.)	2

Appendix Table 2 con't. *Item checklist for assessment of randomized controlled trials of IPM techniques utilizing IPM – QRB.*

		Scoring
VI.	ALLOCATION CONCEALMENT	
17.	Concealed Treatment Allocation	
	Poor concealment of allocation (open enrollment) or inadequate description of concealment	0
	Concealment of allocation with borderline or good description of the process with probability of failure of concealment	1
	High quality concealment with strict controls (independent assignment without influence on the assignment sequence)	2
VII.	BLINDING	
18.	Patient Blinding	
	Patients not blinded	0
	Patients blinded adequately	1
19.	Care Provider Blinding	
	Care provider not blinded	0
	Care provider blinded adequately	1
20.	Outcome Assessor Blinding	
	Outcome assessor not blinded or was able to identify the groups	0
	Performed by a blinded independent assessor with inability to identify the assignment-based provider intervention (i.e., subcutaneous injection, intramuscular distant injection, difference in preparation or equipment use, numbness and weakness, etc.)	1
VIII.	CONFLICTS OF INTEREST	
21.	Funding and Sponsorship	
	Trial included industry employees	-3
	Industry employees involved; high levels of funding with remunerations by industry or an organization funded with conflicts	-3
	Industry or organizational funding with reimbursement of expenses with some involvement	0
	Industry or organization funding of expenses without involvement	1
	Funding by internal resources only with supporting entity unrelated to industry	2
	Governmental funding without conflict such as NIH, NHS, AHRQ	3
22.	Conflicts of Interest	
	None disclosed with potential implied conflict	0
	Marginally disclosed with potential conflict	1
	Well disclosed with minor conflicts	2
	Well disclosed with no conflicts	3
	Hidden conflicts with poor disclosure	–1
	Misleading disclosure with conflicts	–2
	Major impact related to conflicts	–3
TOTAL		48

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. *Methodological quality assessment of randomized trials of epidural injections in lumbar radiculopathy or sciatica utilizing Cochrane review criteria.*

	Manchikanti et al (45)	Ackerman & Ahmad (55)	Dashfield et al (56)	Murakibhavi & Khemka (46)	Kamble et al (57)	Pandey (58)	Singh et al (59)	Manchikanti et al (47)
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 (48)	Ökmen & Ökmen (49)	Rados et al (60)	Ghai et al (61)	Candido et al (62)	Amr (63)	Karppinen et al (50)	Manchikanti et al (51)
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

Appendix Table 3 con't. *Methodological quality assessment of randomized trials of epidural injections in lumbar radiculopathy or sciatica utilizing Cochrane review criteria.*

	Ghai et al (48)	**Ökmen & Ökmen (49)**	**Rados et al (60)**	**Ghai et al (61)**	**Candido et al (62)**	**Amr (63)**	**Karppinen et al (50)**	**Manchikanti et al (51)**
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

Y = Yes; N = No; U = Unclear

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 3 con't. *Methodological quality assessment of randomized trials of epidural injections in lumbar radiculopathy or sciatica utilizing Cochrane review criteria.*

	Riew et al (52,53)	Tafazal et al (54)	Vad et al (64)	Jeong et al (65)	Kennedy et al (66)
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

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 4. *Methodologic quality assessment of randomized trials of epidural injections in lumbar radiculopathy or sciatica utilizing IPM – QRB.*

		Manchikanti et al (45)	Ackerman & Ahmad (55)	Dashfield et al (56)	Murakibhavi & Khemka (46)	Kamble et al (57)	Pandey (58)	Singh et al (59)	Manchikanti et al (47)
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

Appendix Table 4 con't. *Methodologic quality assessment of randomized trials of epidural injections in lumbar radiculopathy or sciatica utilizing IPM – QRB (continued).*

		Manchikanti et al (45)	Ackerman & Ahmad (55)	Dashfield et al (56)	Murakibhavi & Khemka (46)	Kamble et al (57)	Pandey (58)	Singh et al (59)	Manchikanti et al (47)
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

		Ghai et al (48)	Ökmen & Ökmen (49)	Rados et al (60)	Ghai et al (61)	Candido et al (62)	Amr (63)	Karppinen et al (50)	Manchikanti et al (51)
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 4 con't. ***Methodologic quality assessment of randomized trials of epidural injections in lumbar radiculopathy or sciatica utilizing IPM – QRB.***

		Riew et al (52,53)	**Tafazal et al (54)**	**Vad et al (64)**	**Jeong et al (65)**	**Kennedy et al (66)**
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

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 5. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar radiculopathy or sciatica.*

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.**	
TRANSFORAMINAL											
Karppinen et al, 2001 (50) 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 (51) 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 (52,53) 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 5 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar radiculopathy or sciatica.*

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.**	
Tafazal et al, 2009 (54) 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 (55) 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 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar radiculopathy or sciatica.*

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.**	
Kamble et al, 2016 (57) 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 (58) 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 5 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar radiculopathy or sciatica.*

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 (60) 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 (61) 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 (64) 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 5 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in transforaminal epidural injections in lumbar radiculopathy or sciatica.*

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.**	
Jeong et al, 2007 (65) 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 (66) 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

Appendix Table 6. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in caudal epidural injections in lumbar radiculopathy or sciatica.*

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											
Manchikanti et al, 2012 (45) 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 (46) 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 (55) 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 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in caudal epidural injections in lumbar radiculopathy or sciatica.*

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											
Dashfield et al, 2005 (56) 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 (57) 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 (58) 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 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in caudal epidural injections in lumbar radiculopathy or sciatica.*

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											
Singh et al, 2017 (59) 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

Appendix Table 7. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar radiculopathy or sciatica.*

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.**	
INTERLAMINAR											
Manchikanti et al, 2014 (47) 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 (48) 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 7 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar radiculopathy or sciatica.*

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.**	
INTERLAMINAR											
Ökmen & Ökmen 2017 (49) 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 (55) 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 (57) 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 7 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar radiculopathy or sciatica.*

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.**	
INTERLAMINAR											
Pandey, 2016 (58) 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.
Rados et al, 2011 (60) 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 (61) 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.

Appendix Table 7 con't. *Characteristics of fluoroscopic randomized trials of conservative or placebo or local anesthetic, or local anesthetic and steroids in interlaminar epidural injections in lumbar radiculopathy or sciatica.*

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.**	
INTERLAMINAR											
Candido et al, 2013 (62) 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.
Amr, 2011 (63) 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

Appendix Table 8. *Characteristics of comparative fluoroscopic epidural injections in lumbar radiculopathy or sciatica.*

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.	
CAUDAL VERSUS INTERLAMINAR											
Ackerman & Ahmad, 2007 (55) 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 (57) 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 (58) 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 8 con't. *Characteristics of comparative fluoroscopic epidural injections in lumbar radiculopathy or sciatica.*

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.	
CAUDAL VERSUS TRANSFORAMINAL											
Ackerman & Ahmad, 2007 (55) 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 (57) 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 (58) 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 8 con't. *Characteristics of comparative fluoroscopic epidural injections in lumbar radiculopathy or sciatica.*

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.	
Singh et al, 2017 (59) 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 (55) 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 8 con't. *Characteristics of comparative fluoroscopic epidural injections in lumbar radiculopathy or sciatica.*

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.	
Kamble et al, 2016 (57) 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 (58) 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.
Rados et al, 2011 (60) 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

Appendix Table 8 con't. *Characteristics of comparative fluoroscopic epidural injections in lumbar radiculopathy or sciatica.*

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.	
Ghai et al, 2014 (61) 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