Systematic Review

Caudal Epidural Injections in the Management of Chronic Low Back Pain: A Systematic Appraisal of the Literature

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Background: Epidural injections with local anesthetics and steroids are one of the most commonly used interventions in managing chronic low back pain and lower extremity pain of various causes. However, despite their extensive use, debate continues on their effectiveness due to the lack of well-designed, randomized, controlled studies to determine the effectiveness of epidural injections in general, and caudal epidural injections in particular.

Study Design: A systematic review of caudal epidural injections with or without steroids in managing chronic pain secondary to lumbar disc herniation or radiculitis, post lumbar laminectomy syndrome, spinal stenosis, and discogenic pain without disc herniation or radiculitis.

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

Methods: The available literature on caudal epidural injections with or without steroids in managing various types of chronic low back pain with or without lower extremity pain was reviewed. The quality assessment and clinical relevance criteria utilized were the Cochrane Musculoskeletal Review Group criteria as utilized for interventional techniques for randomized trials and the criteria developed by the Newcastle-Ottawa Scale criteria for fluoroscopic observational studies.

The level of evidence was classified as good, fair, or poor based on the quality of evidence developed by the U.S. Preventive Services Task Force (USPSTF). Data sources included relevant literature identified through searches of PubMed and EMBASE from 1966 to December 2011, and manual searches of the bibliographies of known primary and review articles.

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

Results: For this systematic review, 73 studies were identified. Of these, 51 were excluded and a total of 16 studies met inclusion criteria for methodological quality assessment with 11 randomized trials and 5 non-randomized studies.

For lumbar disc herniation, the evidence is good for short- and long-term relief of chronic pain secondary to disc herniation or radiculitis with local anesthetic and steroids and fair relief with local anesthetic only. In managing chronic axial or discogenic pain, spinal stenosis, and post surgery syndrome, the indicated evidence is fair.

Limitations: The limitations of this study include the paucity of literature, specifically for chronic pain without disc herniation.

Conclusion: There was good evidence for short- and long-term relief of chronic pain secondary to disc herniation or radiculitis with local anesthetic and steroids and fair relief with local anesthetic only. Further, this systematic review also provided indicated evidence of fair for caudal epidural injections in managing chronic axial or discogenic pain, spinal stenosis, and post surgery syndrome.

Key words: Chronic low back pain, lower extremity pain, lumbar disc herniation, lumbar radiculitis, lumbar discogenic pain, post lumbar laminectomy or surgery syndrome, spinal stenosis, caudal epidural injections, steroids, local anesthetic

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Chronic low back pain arising from various structures of the spine constitutes the majority of the pain problems in the United States and across the world (1-8). With the increasing prevalence of chronic persistent low back pain, numerous modalities of treatments applied to manage chronic low back pain are also exploding (1,9-43). In the United States, epidural injections are one of the most commonly utilized modalities of treatment in managing chronic low back pain and lower extremity pain, in addition to numerous other modalities including surgical interventions (14-43). Epidural injections are administered by accessing the lumbar epidural space by multiple routes including caudal, transforaminal, and interlaminar. While significant differences have been described between these 3 approaches, with the caudal approach, multiple advantages include being target specific for a lower levels, thus reaching the primary site of pathology, its ability to reach the ventrolateral epidural space in a significant proportion of patients, and that it can be safely performed in cases of post surgery syndrome with hardware, etc. (1,28,30,32,39,40,44-55).

Interlaminar entry is considered to deliver the medication closely to the assumed site of pathology, and while the transforaminal approach is considered the target-specific modality requiring the smallest volume to reach the primary site of pathology (1,28). Caudal epidurals are considered as the safest and easiest, with minimal risk of inadvertent dural puncture, even though requiring relatively high volumes (1,28). In the past, caudal epidural injections have been shown to be effective when compared to interlaminar epidural injections (1,28,30-32,46-49,56). However, the recent literature has shown that while caudal epidural injections may not be superior to either interlaminar or transforaminal, they may provide equal effectiveness (1,28,30-32,56-89). Even then, vigorous debate continues with regards to the medical necessity and indications of lumbar epidural injections (14,20,27,28,31,32,40,50). Multiple systematic reviews, guidelines, health technology assessments, and local medical coverage decisions, have been published (1,14,20,28,30-32,40,50,71,72,90-93). The evidence was highly variable from indeterminate to strong in various publications (1,14,20,28,30-32,40,48-50). Further, the benefit and most effective route of administration for epidural steroids continues to be debated (1,14,20,28,30-32,48-50).

Kuslich et al (94) identified intervertebral discs, facet joints, ligaments, fascia, muscles, and nerve root dura as tissues capable of transmitting pain in the low back. Chronic low back and lower extremity pain may be transmitted by either intervertebral discs, facet joints, ligaments, fascia, muscles, sacroiliac joint, and nerve root dura, the tissues capable of transmitting pain in the low back (1,94,95). Chronic, persistent low back, lower extremity pain and radicular pain may be secondary to either disc herniation, discogenic pain, spinal stenosis, or postlumbar surgery syndrome resulting in disc related pain with or without radiculitis.

Conn et al (28) for therapeutic caudal epidural steroid injections evaluated multiple studies utilizing Cochrane Musculoskeletal Review group criteria with criterial of short-term relief as less than 6 months and long-term relief for greater than 6 months, showing Level I evidence of short- and long-term relief in managing chronic and lower extremity pain secondary to lumbar disc herniation and/or radiculitis, and discogenic pain without disc herniation or radiculitis. However, the indicated evidence was Level II-I or II-II for caudal epidural injections in managing low back pain of postlumbar laminectomy syndrome and spinal stenosis. In contrast, Chou and Huffman (20) combined interlaminar and caudal epidural injections into one category reaching erroneous conclusions that these treatments were only effective for short-term relief in radiculopathy. However, in a critical evaluation of American Pain Society (APS) guidelines (20), Manchikanti et al (32), with updated evidence utilizing the same criteria as Chou and Huffman, with grading of good, fair, and poor, concluded that there was fair evidence for the therapeutic effectiveness of caudal epidural injections in patients with disc herniation or radiculitis with or without steroids for short-term and long-term relief. Further, they also showed the evidence was good for therapeutic effectiveness of caudal epidural injections in disc herniation or radiculitis. Further, the reevaluation by Manchikanti et al (32) with the addition of new studies also showed fair evidence for post surgery syndrome, spinal stenosis, and discogenic pain without disc herniation.

Peterson and Hodler (71), evaluating multiple systematic reviews (28,48,49), concluded that a caudal approach was the most effective for epidural injection of corticosteroids into the lumbar region. Rho and Tang (72), in describing the efficacy of lumbar epidural steroid injections which also included all 3 approaches, showed good evidence for caudal epidural, however, inferior to transforaminal epidural injections. Further, multiple other evaluators in the past have reached favorable conclusions with moderate effectiveness in

managing lumbar radiculopathy, when these were separated from blind interlaminar epidural injections.

The objective of this systematic review is to determine the effects of caudal epidural injections with or without steroids, with or without fluoroscopy, and for various conditions including disc herniation, spinal stenosis, discogenic pain, and post lumbar surgery syndrome. The objectives also included the evaluation of short-term, as well as long-term pain relief, with improvement in functional status.

1.0 Methods

The methodology utilized in this systematic review followed the review process derived from evidence-based systematic reviews and meta-analysis of randomized trials and observational studies (1,14,96-104), Consolidated Standards of Reporting Trials (CONSORT) guidelines for the conduct of randomized trials (105,106), Standards for Reporting Observational Studies (STROBE) (107), Cochrane guidelines (14,102,103), Chou and Huffman's guidelines (20), and quality of reporting of analysis (99).

1.1 Criteria for Considering Studies for This Review

1.1.1 Types of Studies

Randomized controlled trials
Non-randomized observational studies
Case reports and reviews for adverse effects

1.1.2 Types of Participants

Participants of interest were adults aged at least 18 years with chronic low back and lower extremity pain of at least 3 months duration.

Participants must have failed previous pharmacotherapy, exercise therapy, etc., prior to starting interventional pain management techniques.

1.1.3 Types of Interventions

The interventions were caudal epidural injections for chronic low back and/or lower extremity pain. All randomized trials with proper inclusion criteria and appropriately performed non-randomized studies with proper technique under image guidance were included.

1.1.4 Types of Outcome Measures

- The primary outcome parameter was pain relief.
- The secondary outcome measures were functional improvement; change in psychological status; return to work; reduction or elimination of opioid use, other drugs, or other interventions; and complications.
- At least 2 of the review authors independently, in an unblinded standardized manner, assessed the outcomes measures. Any disagreements between reviewers were resolved by a third author and consensus.

1.2 Literature Search

Searches were performed from the following sources without language restrictions:

1. PubMed from 1966
   www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed
2. EMBASE from 1980
   www.embase.com
3. Cochrane Library
   www.thecochranelibrary.com/view/0/index.html
4. U.S. National Guideline Clearinghouse (NGC)
   www.guideline.gov
5. Previous systematic reviews and cross references
6. Clinical Trials
   clinicaltrials.gov

The search period was from 1966 to December 2011.

1.3 Search Strategy

The search strategy emphasized chronic low back and lower extremity pain, disc herniation, discogenic pain, post lumbar laminectomy syndrome, spinal stenosis, and radiculitis treated with caudal epidural injections.

At least 2 of the review authors independently, in an unblinded standardized manner, performed each search. Accuracy was confirmed by a statistician. All searches were combined to obtain a unified search strategy. Any disagreements between reviewers were resolved by a third author and consensus.

1.4 Data Collection and Analysis

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

and case reports were excluded.

1.4.1 Selection of Studies

- In an unblinded, standardized manner, 2 review authors screened the abstracts of all identified studies against the inclusion criteria.
- All articles with possible relevance were then retrieved in full text for comprehensive assessment of internal validity, quality, and adherence to inclusion criteria.

1.4.2 Inclusion and Exclusion Criteria

The following are the inclusion and exclusion criteria:

1. Are the patients described in sufficient detail to allow one to decide whether they are comparable to those who are treated in interventional pain management clinical practices?
   A. Setting – office, hospital, outpatient, inpatient
   B. Physician – interventional pain physician, general physician, anesthesiologist, physiatrist, neurologist, rheumatologist, orthopedic surgeon, neurosurgeon, etc.
   C. Patient characteristics - duration of pain
   D. Non-interventional techniques or surgical intervention in the past
2. Is the intervention described in sufficient detail to enable one to apply its use to patients in interventional pain management settings?
   A. Nature of intervention
   B. Frequency of intervention
   C. Duration of intervention
3. Were clinically relevant outcomes measured?
   A. Proportion of pain relief
   B. Disorder/specific disability
   C. Functional improvement
   D. Allocation of eligible and non-eligible patients to return to work
   E. Ability to work

1.4.3 Clinical Relevance

The clinical relevance of the included studies were evaluated according to 5 questions recommended by the Cochrane Back Review Group (Table 1) (101,108). Each question was scored as positive (+) if the clinical relevance item was met, negative (–) if the item was not met, and unclear (?) if data were not available to answer the question.

1.4.4 Methodological Quality or Validity Assessment

Even though none of these instruments or criteria have been systematically assessed, the advantages and disadvantages of each system were debated.

The methodological quality assessment was performed by 2 review authors who independently assessed, in an unblinded standardized manner, the internal validity of all the studies.

Any discrepancies or conflicts were arbitrated by a third reviewer to either reach a consensus agreement or break a tie. If there was a conflict of interest with the reviewed manuscripts with authorship or any other type of conflict, the involved authors did not review the manuscripts for quality assessment or evidence synthesis.

The quality of each individual article used in this analysis was assessed by Cochrane review criteria (Table 2) (102) for randomized trials, and Newcastle-Ottawa

Table 1. *Clinical relevance questions*.

	P (+)	N (-)	U (unclear)
A) Are the patients described in detail so that one can decide whether they are comparable to those who are treated in clinical practice?			
B) Are the interventions and treatment settings described in sufficient detail to apply its use in clinical practice?			
C) Were clinically relevant outcomes measured and reported?			
D) Is the size of the effect clinically meaningful?			
E) Do the likely treatment benefits outweigh the potential harms?			

Scoring adapted and modified from Staal JB, et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (108).

Table 2. ***Randomized controlled trials quality rating system.***

A	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, pre-ordered sealed envelopes, sequentially-ordered vials, telephone call to a central office, and pre-ordered list of treatment assignments. 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.	Yes/No/Unsure
B	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
C	Was knowledge of the allocated interventions adequately prevented during the study?		
	3. Was the patient blinded to the intervention?	This item should be scored "yes" if the 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
	4. Was the care provider blinded to the intervention?	This item should be scored "yes" if the 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
	5. Was the outcome assessor blinded to the intervention?	Adequacy of blinding should be assessed for the primary outcomes. This item should be scored "yes" if the success of blinding was tested among the outcome assessors and it was successful or: –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., co-interventions, 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.	Yes/No/Unsure
D	Were incomplete outcome data adequately addressed?		
	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.	Yes/No/Unsure
	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 non-compliance and co-interventions.	Yes/No/Unsure
E	8. Are reports of the study free of suggestion of selective outcome reporting?	In order to receive a "yes," the review author determines if all the results from all pre-specified 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
F	Other sources of potential bias:		
	9. Were the groups similar at baseline regarding the most important prognostic indicators?	In order to receive a "yes," 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

Table 2 (cont.). ***Randomized controlled trials quality rating system.***

	10. Were co-interventions avoided or similar?	This item should be scored "yes" if there were no co-interventions or they were similar between the index and control groups.	Yes/No/Unsure
	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 over 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
	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 important outcome assessments.	Yes/No/Unsure

Adapted and Modified: Furlan AD, Pennick V, Bombardier C, van Tulder Ml; Editorial Board, Cochrane Back Review Group. 2009 updated method guidelines for systematic reviews in the Cochrane Back Review Group. *Spine (Phila Pa 1976)* 2009; 34:1929-1941 (109)

Table 3. ***Newcastle-Ottawa quality assessment scale: Case control studies.***

Selection
1) Is the case definition adequate? a) yes, with independent validation* b) yes, e.g. record linkage or based on self reports c) no description
2) Representativeness of the cases a) consecutive or obviously representative series of cases * b) potential for selection biases or not stated
3) Selection of Controls a) community controls * b) hospital controls c) no description
4) Definition of Controls a) no history of disease (endpoint) * b) no description of source
Comparability
1) Comparability of cases and controls on the basis of the design or analysis a) study controls for _____ (Select the most important factor.) * b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)
Exposure
1) Ascertainment of exposure a) secure record (e.g. surgical records) * b) structured interview where blind to case/control status * c) interview not blinded to case/control status d) written self report or medical record only e) no description
2) Same method of ascertainment for cases and controls a) yes * b) no
3) Non-Response rate a) same rate for both groups * b) non respondents described c) rate different and no designation

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of 2 stars can be given for Comparability.

Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (109).

Table 4. *Newcastle-Ottawa quality assessment scale for cohort studies.*

Selection
1) Representativeness of the exposed cohort a) truly representative of the average _____ (describe) in the community * b) somewhat representative of the average _____ in the community c) selected group of users (e.g. nurses, volunteers) d) no description of the derivation of the cohort
2) Selection of the non exposed cohort a) drawn from the same community as the exposed cohort * b) drawn from a different source c) no description of the derivation of the non exposed cohort
3) Ascertainment of exposure a) secure record (e.g. surgical records)* b) structured interview * c) written self report d) no description
4) Demonstration that outcome of interest was not present at start of study a) yes * b) no
Comparability
1) Comparability of cohorts on the basis of the design or analysis a) study controls for _____ (select the most important factor) * b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)
Outcome
1) Assessment of outcome a) independent blind assessment * b) record linkage * c) self report d) no description
2) Was follow-up long enough for outcomes to occur a) yes (select an adequate follow-up period for outcome of interest) * b) no
3) Adequacy of follow up of cohorts a) complete follow-up — all subjects accounted for * b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow-up, or description provided of those lost) * c) follow-up rate < ____% (select an adequate %) and no description of those lost d) no statement

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.
Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (109).

Scale for observational studies (Tables 3 and 4) (109). For nonrandomized observational studies, the patient population should have had at least 50 total or at least 25 in each group if they were comparison groups and must have been performed under fluoroscopic guidance.

For adverse effects, confounding factors, etc., it was not possible to use quality assessment criteria. Thus, these were considered based on interpretation of the reports published and critical analysis of the literature.

Only the randomized trials meeting the inclusion criteria with at least 6 of 12 criteria were utilized for analysis. However, studies scoring lower were described and provided with an opinion and critical analysis.

Observational studies had to meet a minimum of 7 of the 13 criteria for cohort studies and 5 of 10 for case-control studies. Studies scoring less were also described and provided with an opinion and a critical analysis.

If the literature search provided at least 5 randomized trials meeting the inclusion criteria and they were homogenous for each modality and condition evaluated, a meta-analysis was performed.

All caudal epidural injections were also evaluated separately for disc herniation, discogenic pain, spinal stenosis, and post surgery syndrome.

1.4.5 Data Extraction and Management

Two review authors independently, in an unblinded standardized manner, extracted the data from the included studies. Disagreements were resolved by discussion between the 2 reviewers; if no consensus could be reached, a third author was called in to break the impasse.

1.4.6 Assessment of Heterogeneity

Whenever meta-analyses were conducted, the I-squared (I2) statistic was used to identify heterogeneity (110). Combined results with I2 > 50% were considered substantially heterogenous.

Analysis of the evidence was based on the condition (i.e., disc herniation or spinal stenosis) to reduce any clinical heterogeneity.

1.4.7 Measurement of Treatment Effect in Data Synthesis (Meta-Analysis)

Data were summarized using meta-analysis when at least 5 studies per type of disorder were available that met the inclusion criteria (e.g., lumbar disc herniation or spinal stenosis, etc.).

Qualitative (the direction of a treatment effect) and quantitative (the magnitude of a treatment effect) conclusions were evaluated. Random-effects meta-analysis to pool data was also used (111).

The minimum amount of change in pain score to be clinically meaningful has been described as a 2-point change on a scale of 0 to 10 (or 20 percentage points), based on findings in trials studying general chronic pain (112), chronic musculoskeletal pain (113), and chronic low back pain (96,99,101,113-115), which have been commonly utilized. However, recent descriptions of clinically meaningful improvement showed either pain relief or functional status as 50% (59-65,85-89,116-124). Consequently, for this analysis, we utilize clinically meaningful pain relief of at least a 3-point change on an 11-point scale of 0 to 10, or 50% pain relief from the baseline, as clinically significant and functional status improvement of 40% or more.

1.4.8 Integration of Heterogeneity

The evidence was assessed separately by administration to each condition. The meta-analysis was performed only if there were at least 5 studies meeting inclusion criteria available for each variable.

Statistical heterogeneity will be explored using univariate meta-regression (125).

1.4.9 Software Used for Measurement

The data were analyzed using SPSS Version 9.0.1 statistical software (SPSS Inc., Chicago, IL), Microsoft Access 2003, and Microsoft Excel 2003 (Microsoft Corporation, Redmond, WA).

Meta-analyses were performed with Comprehensive Meta-Analysis Software Version 2.0 for Windows (Biostat Inc., Englewood, NJ) (126).

1.5 Summary Measures

Summary measures included 50% or more reduction of pain in at least 40% of the patients, or at least a 3-point decrease in pain scores and a relative risk of adverse events including side effects.

1.6 Analysis of Evidence

The analysis of the evidence was performed based on United States Preventive Services Task Force (USP-

Table 5. *Method for grading the overall strength of the evidence for an intervention.*

Grade	Definition
Good	Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes (at least 2 consistent, higher-quality RCTs or studies of diagnostic test accuracy).
Fair	Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, size, or consistency of included studies; generalizability to routine practice; or indirect nature of the evidence on health outcomes (at least one higher-quality trial or study of diagnostic test accuracy of sufficient sample size; 2 or more higher-quality trials or studies of diagnostic test accuracy with some inconsistency; at least 2 consistent, lower-quality trials or studies of diagnostic test accuracy, or multiple consistent observational studies with no significant methodological flaws).
Poor	Evidence is insufficient to assess effects on health outcomes because of limited number or power of studies, large and unexplained inconsistency between higher-quality trials, important flaws in trial design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

Adapted and modified from methods developed by US Preventive Services Task Force (20,127).

STF) criteria as illustrated in Table 5, criteria which has been utilized by multiple authors (127).

The analysis was conducted using 3 levels of evidence ranging from good, fair, and poor.

At least 2 of the review authors independently, in an unblinded standardized manner, analyzed the evidence. Any disagreements between reviewers were resolved by a third author and consensus. If there were any conflict of interest (e.g., authorship), those reviewers were recused from assessment and analysis.

1.7 Outcome of the Studies

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

For observational studies, a study was judged to be positive if the epidural injection therapy was effective, with outcomes reported at the reference point with positive or negative results at one month, 3 months, 6 months, and one year. However, observational studies were only included in the evidence synthesis if there were less than 5 randomized trials meeting inclusion criteria for evidence synthesis for each condition (i.e., disc herniation, spinal stenosis, discogenic pain, and post surgery syndrome).

2.0 Results

Figure 1 shows a flow diagram of study selection as recommended by Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (100). There were 73 studies considered for inclusion (46,47,56-70,73-84,128-171), with 6 duplicate studies (59-62,65,81-83,162,163,166,167).

Of the 73 caudal epidural trials identified, 51 were excluded (46,47,57,58,63,64,66-70,73,78,79,84,128-138,140, 143-145, 148,150-171). Table 6 shows the reasons for exclusion for randomized trials. Table 7 shows excluded fluoroscopically guided observational studies. Of these, only 16 were randomized trials (63,64,66,68,78,84,128,130,135-138,140,162,163,166,167,169) and 19 were non-randomized studies (46,47,57,67,73,79,129,132,134,144,152,154,155, 158,159,164,168,170,171). The remaining 16 non-randomized studies were performed without fluoroscopy (58, 69,70, 131,133,143,145,148,150,151,153,156,157,160,161,165).

Tables 8 and 9 illustrates characteristics of studies considered for inclusion. There were 2 short-term randomized trials (142,146), 13 randomized trials evaluating long-term follow-up (59-62,65,77,80-83,139,141,147), with 4 duplicate studies (59-62,65,81-83), resulting in a total of 9 randomized trials, and 5 non-randomized studies all evaluating long-term outcomes (56,74-76,149). Follow-up of less than 6 months was considered as short-term and 6 months or longer was considered as long-term.

2.1 Clinical Relevance

Of the 16 studies assessed for clinical relevance, all the studies met criteria with scores of 3 of 5 or greater. Table 10 illustrates assessment of clinical relevance.

2.2 Methodological Quality Assessment

A methodological quality assessment of the randomized controlled trials (RCTs) meeting inclusion criteria was carried out utilizing Cochrane review criteria as shown in Table 11. Studies achieving Cochrane scores of 9 or higher were considered as high quality, 6 to 8 were considered as moderate quality, and studies scoring less than 6 were excluded.

There were 2 randomized trials evaluating a short-term response of less than 6 months (142,146) with one scoring high quality (142) and one scoring moderate quality (146).

There were 9 randomized trials (59-62,77,80,139,141,147) (after combining duplicates [59-62,65,81-83]) evaluating long-term response of 6 months or longer, with 6 trials considered high quality (59-62,80,147), 2 trials considered moderate quality (77,141), and one trial considered low quality (139).

A methodological quality assessment of the observational studies meeting inclusion criteria was carried out utilizing Newcastle-Ottawa Scales as illustrated in Tables 12 and 13. For cohort studies, studies achieving scores of 10 or higher were considered high quality; 7 to 9 were considered moderate quality; studies scoring less than 7 were considered low quality and were excluded.

For case-control studies, 8 or higher was considered as high quality, 5 to 7 was considered as moderate quality, and less than 5 was considered low quality and those studies were excluded.

There were 5 non-randomized or observational studies including case reports evaluating long-term ef-

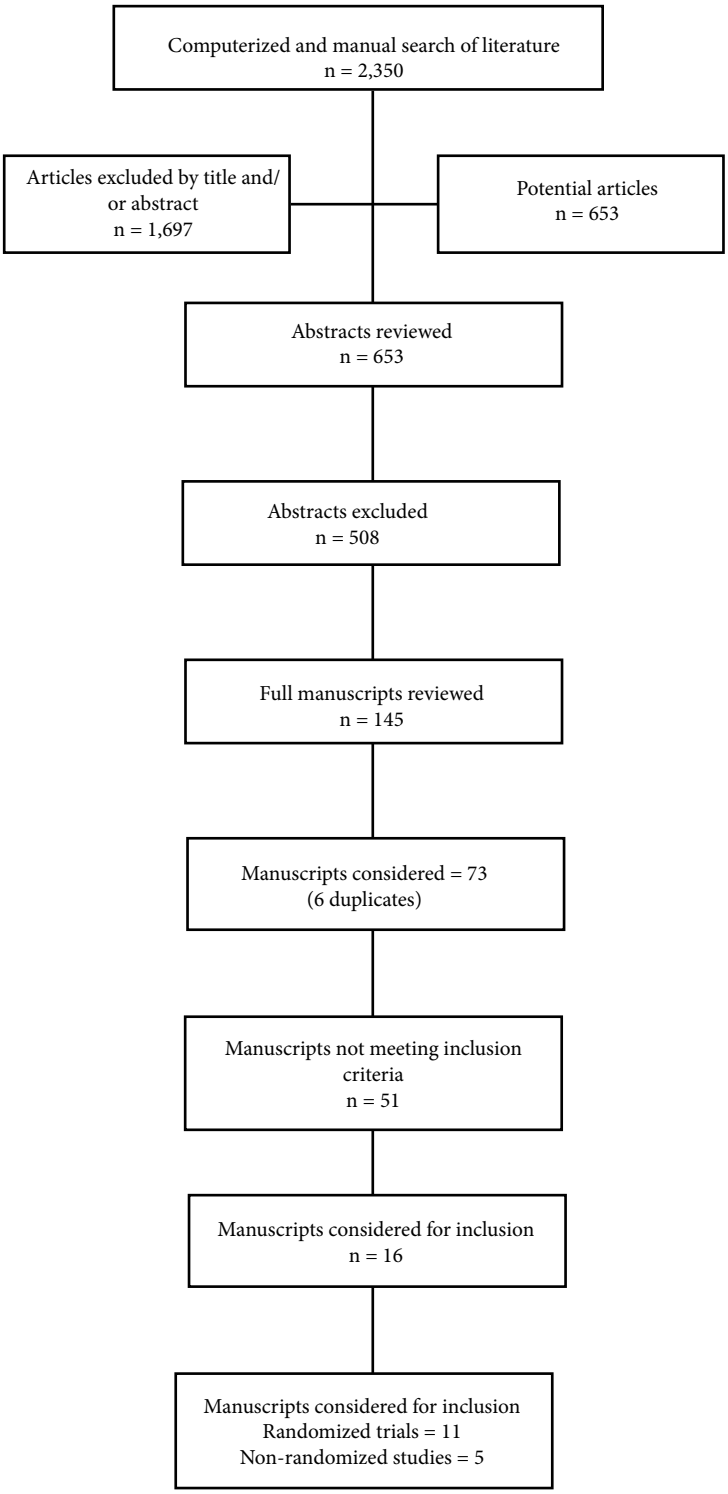

Fig. 1. ***Flow diagram illustrating published literature evaluating caudal epidural injections.***

Table 6. *List of excluded randomized trials*..

Manuscript Author(s)	Condition Studied	Number of Patients	Reason for Exclusion	
			Follow-up Period	Other Reason(s)
Manchikanti et al (63)	Spinal stenosis	50	One-year	Caudal epidural was used as a control in patients who have already failed previous fluoroscopically directed epidural injections.
Manchikanti et al (64)	Lumbar post surgery syndrome	120	One-year	Caudal epidural was used as a control in patients who have already failed previous fluoroscopically directed epidural injections.
Cleary et al (66)	Chronic low back pain	52	NA	Evaluation of flow patterns based on positioning.
Sayegh et al (68)	Disc herniation	183	One-year	Duration of pain was only1-2 months.
Manchikanti et al (78)	Low back pain without disc herniation or radiculitis	62	6 months	Patients with positive provocation discography were only 17.
Dureja et al (84)	Post herpetic neuralgia	50	12 weeks	Spinal pain was not studied.
Zahaar (128)	Lumbar neural compression syndromes	63	one year	High volume injections of local anesthetic and sodium chloride solution with or without steroids blindly. All the patients were with acute herniated nucleus pulposus or spinal stenosis.
Czarski (130)	Sciatica	NA	NA	Inability to obtain the full manuscript. The study was published in 1965.
Laiq et al (135)	Acute lumbar radiculopathy	50	6 months	Patients with acute and subacute pain were included without fluoroscopy.
Mathews et al (136)	Radiculitis	57	One-year	Patients with acute and subacute pain were included.
Breivik et al (137)	Disc herniation, arachnoiditis, and normal MRI findings	35	6 months	Small number of patients with excessive volumes of injectate (> 120 mL).
Bush & Hillier (138)	Unilateral sciatica	23	4 weeks	Small number of patients with 33% of patients (i.e., 4 of 12) in active group and 27% of the patients in placebo group (3 of 11) with acute pain.
Hesla & Breivik (140)	Disc herniation and post surgery syndrome	69	One-year	Small number of patients with excessive volumes of injectate (> 120 mL).
Manchikanti et al (162,166)	Predominantly post surgery syndrome	75	One-year	Caudal epidural was used as a control in patients who have already failed previous fluoroscopically directed epidural injections.
Manchikanti et al (163,167)	Chronic refractory low back and lower extremity pain	83	One-year	Caudal epidural was used as a control in patients who have already failed previous fluoroscopically directed epidural injections.
Manchikanti et al (169)	Lumbar post surgery syndrome and spinal stenosis	NA	NA	Protocol for adhesiolysis

Table 7. *List of excluded fluoroscopic non-randomized studies.*

Manuscript Author(s)	Condition Studied	Number of Patients	Reason for Exclusion	
			Follow-up Period	Other Reason(s)
Manchikanti et al (46)	Chronic low back pain	100	3 days	Evaluation of filling patterns.
Manchikanti et al (47)	All causes of low back pain	100	One-week	A study of evaluation of epidural flow patterns with caudal injection.
Abdulla et al (57)	Post lumbar puncture headache	60	one week	None
Botwin et al (67)	Spinal stenosis	34	One-year	Observational study
Lee et al (73)	Disc herniation or spinal stenosis	233	2 months	Even though the study was performed in 95 patients under fluoroscopy, caudal epidural was performed only in 14 patients.
Manchikanti et al (79)	Chronic low back pain	65	One-year	Only 16 patients in Group 1 and 22 patients in Group II.
Meadeb et al (129)	Post surgery syndrome	47	4 months	Patients were studied 4 months post surgery without randomization.
Anwar et al (132)	Radicular pain or spinal stenosis	40	3 months	Observational study
Bronfort et al (134)	Sciatica	32	12 weeks	Pilot study with 32 patients in 3 groups with acute and subacute pain.
Briggs et al (144)	Spinal stenosis	62	2 years	Lumbar interlaminar and caudal – data unclear
Mitra et al (152)	Spinal stenosis	1	NA	Report of one single case in a patient with spinal stenosis and urinary urgency.
Mohamed et al (154)	L4/5 versus L5/S1 disc prolapse	177	6 months	Evaluation of patients with subacute pain of less than 3 months of duration were included.
Ergin et al (155)	Low back pain	10	NA	Evaluation of accuracy of caudal epidural injection with imaging and the importance of real-time imaging.
Kim et al (158)	Chronic low back pain	32	NA	Evaluation of cephalic spreading levels after volumetric caudal epidural injections.
Price et al (159)	Low back pain	200	NA	Investigation of the accuracy of placement of epidural injection using the lumbar and caudal approaches.
Delport et al (164)	Spinal stenosis	149	Unclear	Confusing data with patients receiving transforaminal, caudal, and combinations.
Manchikanti et al (168)	Spinal stenosis	18	2 years	Percutaneous adhesiolysis was studied.
Manchikanti et al (170)	Post surgery syndrome	120	One-year	Endoscopic adhesiolysis was studied.
Kapural et al (171)	Spinal stenosis	1,000 patient records	8-12 weeks	Various types of epidural injections were evaluated based on the severity of the stenosis.

Table 8. *Assessment of randomized trials for inclusion criteria.*

Manuscript Author(s)	Type of Study	Condition Studied				Number of Patients	Control vs. Intervention or Comparator vs. Treatment	Follow-up Period
		Disc herniation or radiculitis	Discogenic pain without disc herniation	Spinal stenosis	Post Surgery Syndrome			
SHORT-TERM								
McCahon et al (142)	R, AC, B	X	X	X	X	33	Effect of 40 and 80 mg of methylprednisolone was compared mixed with 20 mL mixture of bupivacaine and sodium chloride solution.	12 weeks
Makki et al (146)	R, AC, F	X				57	Patient positioning was studied.	6 weeks
LONG-TERM								
Iversen et al (141)	R, PC, UL	X				116	Subcutaneous Group I placebo was subcutaneous injection of 2 mL of sodium chloride solution injection 0.9% sodium chloride solution injection on sacral hiatus; Group II was given 30 mL of sodium chloride solution into caudal epidural space; Group III was given 30 mL caudal epidural solution with 40 mg of triamcinolone.	52 weeks
Manchikanti et al (59,65)	R, AC, F			X		100	Lidocaine versus lidocaine with steroid with betamethasone.	One-year
Manchikanti et al (60,81)	R, AC, F	X				120	Lidocaine versus lidocaine with steroid with betamethasone.	One-year
Manchikanti et al (61,82)	R, AC, F		X			120	Lidocaine versus lidocaine with steroid with betamethasone.	One-year
Manchikanti et al (62,83)	R, AC, F				X	140	Lidocaine versus lidocaine with steroid with betamethasone.	One-year
Ackerman & Ahmad (77)	R, AC, F	X				90	Caudal versus interlaminar versus transforaminal epidural.	24 weeks
Dashfield et al (80)	R, AC, F	X				60	Caudal epidural versus spinal endoscopic steroids.	6 months
Revel et al (139)	R, AC, B				X	60	Forceful caudal injection: Experimental: 125 mg of prednisolone acetate with 40 mL of normal saline in the treatment group. Control: 125 mg of prednisolone.	6 months
Yousef et al (147)	R, AC, F				X	38	Caudal epidural steroid with local anesthetic and hypertonic saline versus caudal epidural with hypertonic saline, local anesthetic, and hyaluronidase.	52 weeks

Table 9. *Assessment of non-randomized studies for inclusion criteria.*

Manuscript Author(s)	Type of Study	Condition Studied				Number of Patients	Control vs. Intervention or Comparator vs. Treatment	Follow-up Period
		Disc herniation or radiculitis	Discogenic pain without disc herniation	Spinal stenosis	Post Surgery Syndrome			
Manchikanti et al (56)	NR, RE, CC, F	X				225	Blind interlaminar versus fluoroscopically guided caudal versus transforaminal.	One year
Mendoza-Lattes et al (74)	NR, RE, CC, F	X				93	Caudal versus transforaminal	Up to 2 years
Southern et al (75)	RE, F		X*			97	Caudal epidural injection with no control.	28.6 ± 15.6 months
Barre et al (76)	RE, F			X		95	Caudal epidural injection with no control.	6 months
Lee et al (149)	NR, RE, F			X		216	Caudal epidural injection with no control.	1-4 years

*Axial pain with or without disc protrusion

R = Randomized; PC = Placebo control; AC = Active-control; CC = Case-control; NR = Non-randomized; B = Blind; UL = Ultrasound; F = Fluoroscopy; RE = Retrospective; VAS = Visual Analog Scale; VPS = Verbal Pain Score; VNS = Visual Numeric Scale; ODI = Oswestry Disability Index; NRS = Numeric Rating Scale; SF-MPQ = Short-Form McGill Pain Questionnaire; SF-36 = 36-Item Short-Form Health Survey; RMDQ = Roland Morris Disability Questionnaire; HADS = Hospital Anxiety and Depression Scale

Table 10 *Clinical relevance of included studies.*

Manuscript Author(s)	A) Patient description	B) Description of interventions and treatment settings	C) Clinically relevant outcomes	D) Clinical importance	E) Benefits versus potential harms	Total Criteria Met
Manchikanti et al (56)	+	+	+	+	+	5/5
Manchikanti et al (59,65)	+	+	+	+	+	5/5
Manchikanti et al (60,81)	+	+	+	+	+	5/5
Manchikanti et al (61,82)	+	+	+	+	+	5/5
Manchikanti et al (62,83)	+	+	+	+	+	5/5
Mendoza-Lattes et al (74)	+	+	+	+	+	5/5
Southern et al (75)	+	+	+	+	+	5/5
Barre et al (76)	+	+	+	+	+	5/5
Ackerman &Ahmad (77)	+	+	+	+	+	5/5
Dashfield et al (80)	+	+	+	+	+	5/5
Revel et al (139)	+	+	+	+	+	5/5
Iversen et al (141)	+	+	+	-	-	3/5
McCahon et al (142)	+	+	+	+	+	5/5
Makki et al (146)	+	+	+	+	+	5/5
Yousef et al (147)	+	+	+	+	+	5/5
Lee et al (149)	+	+	+	+	+	5/5

+ = Positive; - = Negative ; U = Unclear
Scoring adapted from Staal JB, et al. Injection therapy for subacute and chronic low back pain: An updated Cochrane review. *Spine (Phila Pa 1976)* 2009; 34:49-59 (14).

Table 11. *Methodological quality assessment of randomized trials.*

	Iversen et al (141)	Manchikanti et al (59,65)	Manchikanti et al (60,81)	Manchikanti et al (61,82)	Manchikanti et al (62,83)	Ackerman & Ahmad (77)	Dashfield et al (80)	Revel et al (139)	McCahon et al (142)
Randomization adequate	Y	Y	Y	Y	Y	N	Y	Y	Y
Concealed treatment allocation	Y	Y	Y	Y	Y	N	Y	N	Y
Patient blinded	U	Y	Y	Y	Y	N	Y	N	Y
Care provider blinded	N	Y	N	N	Y	N	N	N	Y
Outcome assessor blinded	U	N	N	N	N	N	N	U	Y
Drop-out rate described	Y	Y	Y	Y	Y	Y	Y	N	Y
All randomized participants analyzed in the group	N	Y	Y	Y	Y	Y	Y	N	N
Reports of the study free of suggestion of selective outcome reporting	Y	Y	Y	Y	Y	Y	Y	Y	Y
Groups similar at baseline regarding most important prognostic indicators	N	Y	Y	Y	Y	Y	Y	Y	Y
Co-interventions avoided or similar	Y	Y	Y	Y	Y	Y	N	Y	Y
Compliance acceptable in all groups	N	Y	Y	Y	Y	Y	Y	N	Y
Time of outcome assessment in all groups similar	Y	Y	Y	Y	Y	Y	Y	Y	Y
Score	6/12	11/12	10/12	10/12	11/12	7/12	9/12	5/12	11/12

Y = Yes; N = no; U = Unclear

fectiveness of caudal epidural injections with follow-up of 6 months or longer (56,74-76,149). Of these, all 5 were considered moderate quality.

Of the included condition-specific studies, 8 studies evaluated or included disc herniation (56,60,74,77,80,81, 141,142,146), with one study with 2 publications (60,81), 2 studies assessed disc-related axial pain without disc herniation or radiculitis or with disc protrusion with axial pain only (61,75,82), with one study with 2 publications (61,82), 3 studies evaluated spinal stenosis (59,65,76,149), with one study with 2 publications (59,65), and 3 studies assessed post surgery syndrome (62,83,139,147), with one study with 2 publications (62,83).

Table 12. *Methodological quality assessment of case control studies.*

	Manchikanti et al (56)	Mendoza-Lattes et al (74)
Selection		
1) Is the case definition adequate?		
a) yes, with independent validation *	X	X
b) yes, e.g. record linkage or based on self reports		
c) no description		
2) Representativeness of the cases		
a) consecutive or obviously representative series of cases *	X	X
b) potential for selection biases or not stated		
3) Selection of controls		
a) community controls *		
b) hospital controls		
c) no description		
4) Definition of controls		
a) no history of disease (endpoint) *		
b) no description of source		
Comparability		
1) Comparability of cases and controls on the basis of the design or analysis		
a) study controls for _____ (Select the most important factor.) *	X	X
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)		
Exposure		
1) Ascertainment of exposure		
a) secure record (e.g., surgical records) *	X	X
b) structured interview where blind to case/control status *		
c) interview not blinded to case/control status		
d) written self report or medical record only		
e) no description		
2) Same method of ascertainment for cases and controls		
a) yes *	X	X
b) no		
3) Non-response rate		
a) same rate for both groups *	X	X
b) non respondents described		
c) rate different and no designation		
SCORE	6/10	6/10

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of 2 stars can be given for Comparability.

Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (109).

Table 13. *Methodological quality assessment of cohort studies.*

	Southern et al (75)	Barre et al (76)	Lee et al (149)
Selection			
1) Representativeness of the exposed cohort	X	X	X
a) truly representative of the average _____ (describe) in the community *			
b) somewhat representative of the average pain patients in the community *			
c) selected group of users, e.g., nurses, volunteers			
d) no description of the derivation of the cohort			
2) Selection of the non exposed cohort			
a) drawn from the same community as the exposed cohort *	X	X	X
b) drawn from a different source			
c) no description of the derivation of the non exposed cohort			
3) Ascertainment of exposure			
a) secure record (e.g., surgical records) *	X	X	X
b) structured interview *			
c) written self report			
d) no description			
4) Demonstration that outcome of interest was not present at start of study			
a) yes *	X	X	X
b) no			
Comparability			
1) Comparability of cohorts on the basis of the design or analysis			
a) study controls for _____ (select the most important factor) *			
b) study controls for any additional factor * (This criteria could be modified to indicate specific control for a second important factor.)			
Outcome (Exposure)			
1) Assessment of outcome			
a) independent blind assessment *			
b) record linkage *			
c) self report	X	X	X
d) no description			
2) Was follow-up long enough for outcomes to occur			
a) yes (select an adequate follow-up period for outcome of interest) *	X	X	X
b) no			
3) Adequacy of follow-up of cohorts			
a) complete follow-up - all subjects accounted for *	X	X	X
b) subjects lost to follow-up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow-up, or description provided of those lost) *			
c) follow-up rate < ____% (select an adequate %) and no description of those lost			
d) no statement			
SCORE	7/13	7/13	7/13

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of 2 stars can be given for Comparability.. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. www.ohri.ca/programs/clinical_epidemiology/oxford.asp (109).

2.3 Meta-Analysis

There were a total of 6 randomized trials evaluating the role of epidural injections in disc herniation (60,77,80,81,141,142,146). Of these, one trial evaluated the effect of saline versus saline with steroid (141), one trial evaluated lidocaine versus lidocaine with betamethasone (60,81), and one trial evaluated dose response of methylprednisolone (142). Among the other 3 studies, one study (77) evaluated caudal versus interlaminar versus transforaminal, whereas a second study (80) evaluated caudal versus endoscopic adhesiolysis and targeted placement of steroid, and one study (146) evaluated patient positioning in assessment of short-term outcomes. Thus, none of the studies met inclusion criteria for meta-analysis with homogeneity for disc herniation.

There was only one randomized trial evaluating discogenic pain without disc herniation (61,82). There was only one randomized trial evaluating spinal stenosis (59,65). There were a total of 3 studies evaluating post surgery syndrome (62,83,139,147). The well-performed active-control trial (62,83) utilized lidocaine alone or lidocaine with betamethasone. The second trial (139) utilized forceful caudal injections in an active-control fashion with essentially no control group utilizing blind methodology and overall low methodological quality assessment. The third trial (147) studied in a small number of patients caudal epidural steroid with local anesthetic and hypertonic saline versus caudal epidural with hypertonic saline versus hyaluronidase. Thus, in none of the categories and none of the groups, meta-analysis was feasible.

2.4 Study Characteristics

Tables 14 and 15 illustrate the study characteristics of the included studies for both randomized trials and non-randomized studies.

2.5 Analysis of Evidence

The evidence was synthesized based on the specific condition for which caudal epidural injection was provided. Table 16 illustrates the results of randomized trials and observational studies of the effectiveness of caudal epidural injections in managing disc herniation of radiculitis; Table 17 illustrates effectiveness in axial or discogenic pain with or without disc herniation or protrusion, without radiculitis, facet joint pain, or SI joint pain; Table 18 illustrates effectiveness in managing spinal stenosis; and Table 19 illustrates effectiveness in managing post surgery syndrome.

2.5.1 Disc Herniation and Radiculitis

There were a total of 8 studies (56,60,74,77,80,81,141,142,146) with one study of 2 publications (60,81), meeting the inclusion criteria evaluating caudal epidural injections in managing disc herniation or radiculitis (Table 16). Thus, 6 randomized trials (60,77,80,81,141,142,146) and 2 non-randomized studies with fluoroscopic utilization (56,74) were included in final analysis. There was only one study by Iversen et al (141) which was of moderate quality utilizing a placebo design; however, without fluoroscopy, but with ultrasound. The study was highly deficient in multiple aspects with substantial criticism advanced (172-177). This study illustrates numerous flaws. As a first concern, the selection criteria are overtly broad. A significant proportion of patients (n = 17) did not even have to undergo randomization because their symptoms improved between assessment and randomization indicating the inclusion of short-term or subacute pain. In addition, after the randomization, 5 patients had spontaneous improvement before the first injection. A large proportion of patients were excluded due to neurologic compression including cauda equina syndrome. They also attributed most of their results to natural course. Patient selection appears to be quite inappropriate. In chronic pain settings with long-lasting pain, patients undergoing various modalities of treatments, would already respond for natural course or placebo effect. Further, while MRI was utilized as the criteria for disc herniation, ultimately the authors included clinically proven radiculopathy for inclusion criteria. Multiple flaws with procedure include ultrasound identification of caudal epidural space, which the authors claim is appropriate for caudal even though they concede it was not appropriate for transforaminal. Ultrasound identification is appropriate for neither caudal nor for transforaminal. Overall, while proponents argue that there is evidence, the accuracy of ultrasound has not been established in adults for interventional techniques (178-183). Further, the injection was not only non-targeted with an unproven technique, namely ultrasound, but also included large volumes of sodium chloride solution without local anesthetics and relatively small volumes of triamcinolone. It also appears somewhat surprising that only 17 patients of the 345 declined to participate in the study, even though it is a placebo-control study. In placebo-controlled trials, patient refusal is one of the most difficult issues researchers have to face. Thus, overall the study failed to take into consideration multiple issues unlike the study with transforaminal

Table14. *Caudal epidural steroid injections either with placebo or active control.*

Study, Year	Number of Patients Selection Criteria	Control	Intervention	Outcome Measures	Time of Measurement	Results	Strengths Weaknesses	Methodological Quality Assessment Score
Iversen et al, 2011 (141)	116 patients with lumbar radiculopathy > 12 weeks	Sham injections of 2 mL 0.9% saline under ultrasound guidance	Caudal epidural injections of 30 mL 0.9% saline Caudal epidural injections of 40 mg of triamcinolone acetonide in 29 mL 0.9% saline Number of injections = 2	ODI, EQLS, VAS	6, 12, and 52 weeks	There was no significant difference in any of the groups evaluated.	Strength: A randomized, placebo-controlled study Weaknesses: Study has numerous deficiencies. This was performed under ultrasound, a large proportion of patients were excluded due to neurological compression including cauda equina syndrome And a significant proportion improved spontaneously.	6/12
McCahon et al, 2011 (142)	33 patients with low back and lower extremity pain due to any cause	40 mg of methylprednisolone mixed with 20 mL of bupivacaine	Methylprednisolone 80 mg mixed with 20 mL bupivacaine	ODI, VAS, HADS	12 weeks	There was significant difference in patients receiving low dose methylprednisolone (i.e., 40 mg).	Strengths: A randomized active-control study Weaknesses: The study has numerous deficiencies including small number of patients which involved all causes which was performed blindly without fluoroscopy.	11/12
Manchikanti et al, 2011 (59,65)	100 patients with diagnosis of spinal stenosis	Caudal epidural injection with 10 mL of lidocaine 0.5%	Caudal epidural with 0.5% lidocaine 9 mL mixed with 1 mL of betamethasone (non-particulate) Number of injections = 1 to 5	NRS, ODI, employment status, opioid intake	3, 6, and 12 months post-treatment	Significant pain relief and functional status improvement, in both groups, 48% in local anesthetic group and 46% in steroid group with better results (60%) in initial successful groups.	Strengths: Well controlled randomized trial. This is the first study utilizing a large number of patients with appropriate randomization and repeat injections based on the relief. Weaknesses: Lack of placebo control	11/12
Manchikanti et al, 2011 (60,81)	120 patients with disc herniation and radiculitis	Caudal epidural with local anesthetic	Caudal epidural steroid with bupivacaine and steroids either methylprednisolone 40 mg, betamethasone, either commercial or preservative free, 6 mg Number of injections = 1 to 5	NRS, ODI, employment status, opioid intake	3, 6, and 12 months post-treatment	Significant pain relief and/or improvement in functional status in 70% and 67% in local anesthetic group and 77% and 75% in steroid group with better results in initial successful group.	Strengths: This is a large controlled evaluation in a practical setting with patients receiving repeat injections based on their relief. Weaknesses: No placebo control	10/12

Table 14 (cont.). *Caudal epidural steroid injections either with placebo or active control.*

Study, Year	Number of Patients Selection Criteria	Control	Intervention	Outcome Measures	Time of Measurement	Results	Strengths Weaknesses	Methodological Quality Assessment Score
Manchikanti et al, 2011 (61,82)	120 patients with chronic low back pain of discogenic origin without facet joint pain, disc herniation, radiculitis and/or SI joint pain.	Caudal epidural with local anesthetic	Caudal epidural with 0.5% lidocaine 9 mL mixed with 1 mL of betamethasone commercial or non-particulate (6 mg) or 40 mg of methylprednisolone, Number of injections = 1 to 5	NRS, ODI, employment status, functional status, opioid intake	3, 6, and 12 months post treatment	Significant pain relief and/or functional status improvement in 55% of the patients in local anesthetic group and 68% of the patients in the steroid group with better results in successful group in > 80% pain relief and over 62% functional status improvement.	Strengths: This is the first study performed in a large proportion of patients in axial or discogenic pain with appropriate randomization, blinding, and repeat of the procedures based on response of the pain. Weaknesses: Lack of placebo control	10/12
Manchikanti et al, 2010 (62,83)	140 patients with low back and lower extremity pain after surgical intervention with post surgery syndrome	Caudal epidural with local anesthetic	Caudal epidural with 9 mL of lidocaine 0.5% mixed with 1 mL of non particulate Celestone. Number of injections = 1 to 5	NRS,ODI, employment status, opioid intake	3, 6, and 12 months post-treatment	Combined pain relief (>/=50%) and disability reduction was recorded in 53% of the patients in the local anesthetic group, and 59% of patients in the local anesthetic and steroid group. Better results in initial successful group.	Strengths: This is the first study performed in a large proportion of patients with post surgery syndrome with appropriate randomization, blinding, and repeat of the procedures based on response of the pain. Weaknesses: Lack of placebo control	11/12
Dashfield et al, 2005 (80)	60 patients with a 6-18 month history of sciatica	Caudal epidural steroid injection with lidocaine 10 mL, 1% with 40 mg of triamcinolone	Spinal endoscopy with lidocaine 10 mL, 1% with 40 mg of triamcinolone Number of injections: 1	Pain relief, SF-MPQ, HAD scores	6 weeks, 3 months, and 6 months	No significant differences were found between the groups for any of the measures at any time. Both techniques benefited patients.	Strengths: Randomized trial with a reasonable proportion of patients performed under fluoroscopy. Weaknesses: No placebo control group and the study compared caudal epidural injection with endoscopy in patients who have never undergone surgical intervention or were diagnosed with epidural fibrosis with only one injection.	9/12

Table 14 (cont.). *Caudal epidural steroid injections either with placebo or active control.*

Study, Year	Number of Patients Selection Criteria	Control	Intervention	Outcome Measures	Time of Measurement	Results	Strengths Weaknesses	Methodological Quality Assessment Score
Revel et al, 1996 (139)	60 patients with persistent or recurrent lumbosciatic pain after surgery, and with epidural fibrosis.	Caudal injection of 125 mg of prednisolone acetate, 5 mL	Forceful caudal injection: 125 mg of prednisolone acetate with 40 mL of normal saline Number of injections: 5	Pain relief, Waddell's, and Main's Functional Score, Schober's test, finger to floor distance, straight leg raising, use of analgesics, satisfaction index, five-level satisfaction index	6 months	The proportion of patients who were relieved of their sciatica was significantly higher in the forceful injection group (n=29; 45%) than in the control group (n=31 19%).	Strengths: Randomized, controlled trial Weaknesses: A small number of patients with unconventional technique of high dose solution blindly without benefit of local anesthetic.	5/12
Makki et al, 2010 (146)	57 patients with low back pain associated with radicular leg pain	Supine position with injection of 10 mL normal saline, 10 mL of 0.5% bupivacaine and 40 mg of methylprednisolone	Group 1 (treatment group) had 28 patients who were placed in the lateral decubitus position after injection, with 10 mL of normal saline, 10 mL of 0.5% bupivacaine, and 40 mg of methylprednisolone Number of Injections: One	VPS, ODI	6 weeks	The degree of improvement in the VPS was significantly greater in lateral decubitus group 1 compared with group 2 (P = 0.00007). The degree of improvement in the ODI was not statistically significant (P = 0.14).	Strengths: Randomized active-control study performed under fluoroscopy Weaknesses: This study has not evaluated the effectiveness of any drug, it rather evaluated the effectiveness of post procedure positioning.	7/12
Yousef et al, 2010 (147)	38 patients with back pain because of failed back surgery syndrome	Fluoroscopically guided caudal epidural steroid, local anesthetic, and hypertonic sodium chloride solution (Group 1)	Fluoroscopically guided caudal epidural steroid, hypertonic saline, local anesthetic, and hyaluronidase (Group 2). Number of injections: 1	VPS, lumbar spine range of motion, opioid intake	6 weeks, 3 months, 6 months and one year.	Significant improvement in short-term pain relief was noted in both groups, while significant long-term pain relief was only achieved in group 2 patients.	Strengths: A prospective randomized double-blind evaluation under fluoroscopy Weaknesses: A small number of patients comparing multiple drugs in each patient.	11/12

ODI = Oswestry Disability Index; VAS = Visual Analog Scale; HADS = Hospital Anxiety and Depression Scale; SF-MPQ = Short-Form McGill Pain Questionnaire; EQLS = European Quality of Life Scale; NRS = Numeric Rating Scale; VPS = Visual Pain Scale

Table 15. *Caudal epidural steroid injections compared with lumbar interlaminar or transforaminal.*

Reference, Year	Number of Patients Selection Criteria	Control	Intervention	Outcome Measures	Time of Measurement	Results	Strengths	Weaknesses	Methodological Quality Assessment Score
Manchikanti et al, 1999 (56)	225 patients receiving epidural injections by 3 routes which included patients with disc herniation, axial low back pain, and post lumbar surgery syndrome	Blind interlaminar	Fluoroscopically guided caudal Number of injections = 4.6 over a period of 2 years	Pain relief of > 50%	Over 12 months	Epidural administration of corticosteroids under fluoroscopy by caudal or transforaminal route was a valuable, safe, and cost-effective technique.	Though this is a retrospective evaluation. Patients were selected randomly from a large number of patients and also evaluated the cost-effectiveness.	This was a retrospective evaluation and the cost-effectiveness was considered as preliminary. Further, there was no homogeneity as lumbar interlaminar were performed without fluoroscopy.	6/10
Mendoza-Lattes et al, 2009 (74)	Retrospective case-control study evaluating 93 patients with lumbar radiculopathy	Transforaminal epidural with 0.25% Marcaine with Depo-Medrol or Celestone either 80 mg or 12 mg	Caudal epidural steroid injections, Marcaine 0.25% mixed with Depo-Medrol 40 mg per mL or Celestone 6 mg per mL with 1.5 to 2 mL solution (up to 18 mg) Number of injections = 1 to 3	VAS, ODI, SF-36. The endpoint was surgical intervention.	Baseline, post treatment (< 6 months), long-term (> 1 year)	The effectiveness of caudal epidural steroid injection was comparable to that of transforaminal epidural steroid injection with approximately 60% of patients improving in both groups.	The authors compared caudal with transforaminal epidural utilizing fluoroscopy.	Non-randomized evaluation	6/10
Ackerman & Ahmad, 2007 (77)	90 patients; L5-S1 disc herniation on imaging and severe S1 radicular pain with S1 radiculopathy on EMG	Fluoroscopically guided interlaminar epidural steroid injection with triamcinolone and saline (n = 30)	Fluoroscopically guided caudal injection with triamcinolone and saline (n = 30) Average injections: 2.5	Numeric pain score (0-10), rating of pain relief, ODI, BDI, contrast dispersion pattern	2, 12, and 24 weeks, postinjection	Transforaminal epidural steroid injection group had significantly more patients with complete and partial relief at 12 and 24 weeks.	Uniform patient selection with all 3 modalities performed under fluoroscopy.	A small number of patients (30) in each group with relatively short duration of follow-up of 24 weeks with differential volumes and lack of blinding, etc.	7/12

ODI = Oswestry Disability Index; VAS = Visual Analog Scale; SF-36 = 36-item Short-Form Health Survey; BDI = Beck Depression Inventory

Table 16. *Results of randomized and observational studies of effectiveness of caudal epidural injections in managing disc herniation or radiculitis.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Interventions	Pain Relief and Function			Results									Comment(s)
					3 mos.	6 mos.	12 mos.	Short-term ≤ 6 mos.			Long-Term > 6 mos.			Long-Term 1 year			
								ST	LA	SAL	ST	LA	SAL	ST	LA	SAL	
Iversen et al (141)	R, PC, UL	6/12	Total = 116	Saline or triamcinolone acetonide with saline Number of injections = 2	N	N	N	U	NA	U	U	NA	U	U	NA	U	Study has numerous deficiencies with flawed design.
Manchikanti et al (60,81)	R, AC, F	10/12	Total = 120	Lidocaine vs. lidocaine mixed with steroid Number of injections = 1 to 5	77% vs. 80%	77% vs. 82%	70% vs. 77%	P	P	NA	P	P	NA	P	P	NA	Positive double-blind randomized trial.
Ackerman & Ahmad (77)	R, AC, F	7/12	Total = 90 Caudal = 30 Interlaminar = 30 Transforaminal =30	methylprednisolone + saline Number of injections=1 to 3	Caudal = 57% Interlaminar = 60% Transforaminal =283%	Caudal = 57% Interlaminar = 60% Transforaminal = 83%	NA	P	NA	NA	P	NA	NA	NA	NA	NA	Relatively short-term follow-up with high volumes of injection.
Dashfield et al (80)	R, AC, F	9/12	Total = 60 Caudal = 30 Endoscopy =30	Lidocaine with triamcinolone Number of injections=1	SI	SI	NA	P	NA	NA	P	NA	NA	NA	NA	NA	Postive in caudal group.
McCahon et al (142)	R, AC, B	11/12	Total = 33	methylprednisolone vs. methylprednisolone with bupivacaine	SI in 40 mg group	NA	NA	P	NA	NA	NA	NA	NA	NA	NA	NA	Very small study
Makki et al (146)	R, AC, F	7/12	Total = 57	Position: supine vs side of leg pain	SI in lateral group	NA	NA	P	NA	NA	NA	NA	NA	NA	NA	NA	Small Study.
Mendoza-Lattes et al (74)	NR, RE, CC, F	6/10	Total = 93 Caudal=39 Transforaminal = 54	Marcaine with depo-medrol Number of injections=1 to 3	VAS 7.4 to 4.4 caudal group, transforaminal 7.9% to 5.7%	Surgery avoided in caudal group -59%, in transforaminal epidural- 55.6%	Surgery avoided in caudal -59%, vs transforaminal - 55.6%	P	NA	NA	P	NA	NA	P	NA	NA	Approx. 60% of the patients improved.

R = Randomized; PC = Placebo Control; AC = Active Control; NR = Non-Randomized; RE = Retrospective; CC = Case Control; UL = Ultrasound; F = Fluoroscopy; B = Blind; P = Positive; N = Negative; NA = Not Applicable; U = Unclear; SI = Significant Improvement; ST = Steroid; LA = Local Anesthetic; SAL = Saline

Table 17. *Results of randomized and observational studies of effectiveness of caudal epidural injections in managing discogenic or axial pain with or without disc herniation or protrusion, without radiculitis, facet joint pain or SI joint pain.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Interventions	Pain Relief and Function			Results									Comment(s)
					3 mos.	6 mos.	12 mos	Short-term ≤ 6 mos.			Long-Term						
											> 6 mos			≥ 1 year			
								ST	LA	SAL	ST	LA	SAL	ST	LA	SAL	
Manchikanti et al (61,82)	R, AC, F	10/12	Total = 120 Lidocaine =60 Lidocaine with steroids = 60	Lidocaine vs. lidocaine mixed with steroidNumber of injections = 1 to 5	87% vs. 88%	89% vs. 93%	84% vs. 85%	P	P	NA	P	P	NA	P	P	NA	Positive randomized double-bline trial.
Southern et al (75)	RE, F	7/13	Total = 97	Betamethasone and lidocaine Number of injections=2 to 4	NA	NA	23%	NA	NA	NA	NA	NA	NA	N	NA	NA	A negative study.

R = Randomized; AC = Active Control; B = Blind; NR = Non-Randomized; RE = Retrospective; PR = Prospective; CC = Case Control; P = Positive; N = Negative; NA = Not Applicable; VAS = Visual Analog Scale; ODI = Oswestry Disability Index; SI = Sacroiliac; IL = Interlaminar; TF = Transforaminal

Table 18. *Results of randomized and observational studies of effectiveness of caudal epidural injections in managing spinal stenosis.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Interventions	Pain Relief and Function			Results									Comment(s)
					3 mos.	6 mos.	12 mos	Short-term ≤ 6 mos.			Long-Term						
											> 6 mos			≥ 1 year			
								ST	LA	SAL	ST	LA	SAL	ST	LA	SAL	
Manchikanti et al (59,65)	R, AC, F	11/12	Total = 100 Lidocaine = 50 Lidocaine + steroid = 50	Lidocaine 0.5% vs. lidocaine mixed with steroid. Number of injections = 1 to 5	66% vs. 62%	58% vs. 56%	48% vs. 46%	P	P	NA	P	P	NA	P	P	NA	Double-blind design in a practical setting.
Barre et al (76)	RE, F	7/13	Total = 95	triamcinolone and preservative free lidocaine Number of injections= 1 to 3	NA	NA	35%	NA	NA	NA	NA	NA	NA	N	NA	NA	Negative outcome study.
Lee et al (149)	NR, RE, F	7/13	Total = 216	Local anesthetic and steroids. Number of injections = 1 to 16	86%	69%	46%	P	NA	NA	P	NA	NA	P	NA	NA	A large study.

R = Randomized; AC = Active Control; NR = Non-randomized; RE = Retrospective; F = Fluoroscopy; P = Positive; N = Negative; NA = Not applicable

Table 19. *Results of randomized trials of effectiveness of caudal epidural injections in managing post surgery syndrome.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Interventions	Pain Relief and Function			Results									Comment(s)
					3 mos.	6 mos.	12 mos.	Short-term ≤ 6 mos.			Long-Term > 6 mos			≥ 1 year			
								ST	LA	SAL	ST	LA	SAL	ST	LA	SAL	
Manchikanti et al (62,83)	R, AC, F	11/12	Total = 140Lidocaine = 70 Lidocaine + steroid = 70	lidocaine vs. lidocaine mixed with non particulate betamethasone Number of injections = 1 to 5	Pain relief 60% vs 69% Function 56% vs 57%	Pain relief 60% vs. 66% Function 56% vs 63%	Pain relief 56% vs. 61% Function 54% vs 61%	P	P	NA	P	P	NA	P	P	NA	Positive results with local anesthetics with or without steroids.
Revel et al (139)	R, AC, B	5/12	Total = 60	Prednisolone acetate and saline or prednisolone alone Number of injections = 6	NA	19% vs 45%	NA	NA	NA	NA	P	NA	NA	NA	NA	NA	Low quality study with positive results.
Yousef et al (147)	R, AC, F	11/12	Total = 38 local anesthetic = 18 hypertonic saline = 20	Local anesthetic, steroids, hypertonic saline, and hyaluronidase Number of injections = 1	85% vs 80%	25% vs 75%	5% vs 45%	P	NA	NA	P	NA	NA	P	NA	NA	Significant improvement in group.

R = Randomized; AC = Active Control; B = Blind; F = Fluoroscopy; P = Positive; N = Negative; NA = Not Applicable

epidural injection under fluoroscopy (184). Ghahreman et al (184), for the first time, have designed and evaluated a true placebo for transforaminal epidural injections and have shown that it is not only the true placebo sodium chloride intramuscular injection, but also intramuscular steroids were ineffective.

Thus, questions with regards to appropriate placebo must be dispelled. Further, the role of placebo substances into active spaces must be realized. The evidence by Ghahreman et al (184) illustrates the evidence that when injected into active structures, sodium chloride solution and local anesthetics are not placebos but generate significant activity (31,32,37,39,40,42,59-65,77,85-89,118-124,141,185-198).

Among the randomized trials, there were only 2 studies which included greater than 100 participants (60,81,141). There was only one placebo-controlled trial (141) and the remaining studies were active control trials (60,80,81,77,142,146). The placebo-controlled trial was flawed (141), even though the accompanying editorial (199) supported the study. Further, active control trials ranged from comparison of local anesthetic versus local anesthetic with steroid, types of steroids, dose response, and finally, caudal were also compared with interlaminar and transforaminal epidural injections.

The populations evaluated in all the included studies were consistent with the inclusion criteria with patients with disc herniation and leg pain. Only the proportion of patients utilized for disc herniation were included (when described) as shown in Table 16, even though, some studies included patients with other conditions.

Among the 6 randomized controlled trials (60,77,80,81,141,142,146), one study (141) utilized placebo with ultrasound showing negative or un-

clear results. Among the remaining 5 active controlled trials (60,77,80,81,142,146), only one trial compared lidocaine with or without steroids (60,81) yielding similar results in short-term and long-term. The second study (80) utilized lidocaine with triamcinolone combination without a lidocaine only group. One study (77), with inclusion of 30 patients in the caudal group, utilized sodium chloride solution with steroid without a local anesthetic group. Thus, in this evaluation, the evidence from only one properly conducted study of lidocaine with or without steroid shows equal results (60,81). Previously, experimental studies (200,201) and multiple other studies have illustrated no significant difference with or without local anesthetic (1,59-65,79,81-83,85-89,120-124). In one study (146), utilizing a mixture of 10 mL of normal saline, 10 mL of 0.5% bupivacaine, and 40 mg of methylprednisolone, the effect of a supine position was compared with a lateral decubitus position after injection, illustrating superior results when the patients were positioned in the lateral decubitus position. However, this study has not evaluated the effectiveness of any drug. Rather this study evaluated the effectiveness of post-procedure positioning. A pilot study of the dose-response of caudal methylprednisolone with levobupivacaine in chronic low back pain evaluated 40 mg and 80 mg of methylprednisolone and concluded that 40 mg appear to be superior to 80 mg when injected in 20 mL levobupivacaine (142).

Among the non-randomized studies, only one study (74) showed positive results, along with avoidance of surgery in the patients undergoing caudal epidural injections. One study (56) illustrated cost-effectiveness of caudal epidural injections with lidocaine and steroids. Further, this study also showed the results of caudal epidural to be equivalent to transforaminal epidural injections.

2.5.1.2 Effectiveness

Of the 6 randomized trials meeting inclusion criteria evaluating caudal epidural steroid injections (60,77,80,81,141,142,146), only 4 of them evaluated long-term results (60,77,80,81,141). There were 2 non-randomized studies (56,74) meeting inclusion criteria evaluating effectiveness of caudal epidural injections, with both of them evaluating long-term effectiveness.

The 4 randomized trials evaluating long-term outcomes (60,77,80,81,141) with 87 patients receiving local anesthetic with steroids (60,80,81) and 60 patients receiving local anesthetic only (60,81) showed positive results. One study (77) utilizing 19 mL sodium chloride solution with 40 mg of methylprednisolone showed positive results. However, the randomized trial with placebo performed under ultrasound guidance showed negative or unclear results (141) utilizing 37 patients in the steroid group with saline. Thus, 3 of the 4 studies evaluating long-term follow-up showed positive results (60,77,80,81), with one of the studies showing negative or unclear results (141). Of these, 2 studies were considered as high quality (60,80,81). The one medium quality showed negative or unclear results (141), whereas the second medium quality study showed positive results (77). Both of them studied mixtures of sodium chloride solution with steroid rather than local anesthetic (77,141). The number of patients included in the positive studies was 177, whereas the single negative or unclear study was 39 patients receiving steroids mixed with sodium chloride solution with similar results whether steroid was injected into the epidural space or over the sacral hiatus.

Among the short-term evaluations, there were 2 additional studies (142,146) both of them showing positive results which utilized local anesthetic and steroids.

Among the non-randomized studies, there were only 2 studies evaluating long-term follow-up (56,74). Of these, one study (74) showed positive long-term results with 39 patients receiving caudal epidural injections. Further, one study (56) evaluated only short-term progress and showed positive or unclear results with local anesthetic and steroid combination.

2.5.2 Axial Pain

Results are illustrated in Table 17. However, there was only one randomized trial (61,82) and one observational study (75) which met the inclusion criteria.

2.5.2.1 Effectiveness

The randomized trial by Manchikanti et al (61,82) as illustrated in Table 17 assessed the effectiveness of caudal epidural injections in axial or discogenic pain without disc herniation and without facet joint or sacroiliac joint pain showing good long-term results. This study utilizing 120 patients, 60 of them receiving local anesthetic and the other 60 receiving local anesthetic with steroid, followed a practical approach repeating the procedures only when the pain had returned and it was necessary with appropriate and practical outcome parameters. Further, this study also utilized controlled comparative local anesthetic blocks, excluded facet joint pain and sacroiliac joint pain prior to starting epidural injections. Thus, it is presumed that the pain is

not related to the posterior structures and it is related to the disc.

The non-randomized study was negative (75). This study evaluated the results only at the end of one year after providing them with epidural injections 2 to 4 in the beginning without any repeat injections and without short-term or mid-term follow-up. Even then, 23% of the patients showed improvement.

2.5.3 Spinal Stenosis

The characteristics of randomized and observational studies of the effectiveness of caudal epidural injections in managing spinal stenosis are illustrated in Table 18.

There was only one randomized trial evaluating the role of spinal stenosis (59,65). The randomized trial (59,65) with positive results was conducted with a practical approach, repeating the procedures only when pain returned. The study also included 100 patients and followed them through one year with appropriate and practical outcome parameters.

There were 2 non-randomized studies (76,149). One study (149) illustrates positive long-term results and the second study (76) showing negative long-term results. However, this study (76) evaluated effectiveness of epidural injections administered one to 3, followed by long-term evaluation without short-term or mid-term evaluations. Even then, it illustrated positive results in 35% of patients at long-term.

2.5.3.1 Effectiveness

The only randomized controlled trial (59,65) included 100 patients with 50 patients in the local anesthetic group and additional 50 patients with local anesthetic and steroids, and showed positive results both short-term and long-term.

One retrospective evaluation (76) with limited results of 1 to 3 injections, available only at one year, which is not expected to provide positive results, showed improvement in 35% of the patients, which may be considered positive even though it does not meet the positive criteria of this evidence synthesis.

The second non-randomized study (149) showed positive results both in short-term and long-term utilization of local anesthetic and steroids.

2.5.4 Post Surgery Syndrome

Table 19 illustrates the results of studies evaluating the effectiveness of caudal epidural injections in managing post surgery syndrome. The studies meeting the inclusion criteria were 2 randomized trials (62,83,139). Of these, one study (62,83) included 140 patients and was performed utilizing CONSORT guidelines as an active control trial. The study also utilized a practical approach in a chronic pain management setting, repeating the injection therapy only with the return of pain. The study showed the results to be superior in patients who were judged to be positive initially.

In contrast, the second study (139) was of low quality utilizing forceful caudal injections with rather high volumes which may not only be uncomfortable but also may be associated with side effects.

Yousef et al (147) evaluated the role of hypertonic sodium chloride solution with steroids with local anesthetic, with or without hyaluronidase, the results illustrating significant improvement in the patients receiving hyaluronidase, thus, this study does not provide any information on local anesthetics with or without steroids.

2.5.4.1 Effectiveness

Of the 3 randomized trials (62,83,139,147), one of them utilized local anesthetic and steroids (62,83), showing positive equivalent results with or without steroids. The second study (139) utilized forceful epidural injections with steroid and 40 mL of sodium chloride solution yielding positive results in the forceful group and negative results with injection of only 2 mL of methylprednisolone. The third study (147) evaluated caudal injections in post surgery syndrome, with assessment of the role of hypertonic sodium chloride solution and also the hyaluronidase. This study illustrated improvement in both groups, but showed superior results when hyaluronidase was utilized. Due to the mixture of multiple drugs with local anesthetic, steroid, hypertonic sodium chloride solution, and hyaluronidase, it is difficult to assess the role of steroids or local anesthetic, but the study does illustrate the effectiveness of hyaluronidase compared to the others.

Thus, the well conducted study, which is under fluoroscopy (62,83) with 140 patients showed positive results, which were equal with local anesthetic alone or with local anesthetic and steroid.

2.6 Level of Evidence

Based on the USPSTF criteria, the evidence was considered at 3 levels – good, fair, and poor.

2.6.1 Lumbar Disc Herniation

For lumbar disc herniation with radiculitis, based

on 3 of 4 positive long-term randomized studies (60,77,80,81), and one negative or unclear conclusion (141), the evidence is considered good for short-term and long-term relief with local anesthetics with steroids.

The sole well conducted randomized trial comparing local anesthetic with steroids (60,81) showed positive results, yielding fair evidence for short- and long-term relief with local anesthetic only.

2.6.2 Axial Pain

The only one well conducted randomized double-blind trial with 120 patients receiving either local anesthetic alone with lidocaine and local anesthetic with steroids showed positive results both in short-term and long-term (61,82).

The second retrospective evaluation (75) showed negative results; however, in this study, patients received 2 to 4 injections in the beginning without any repeat injections and outcomes were assessed after long periods of time without short-term or mid-term follow-up. Even then, 23% of the patients showed significant improvement.

Based on one randomized trial (82), the evidence is fair for caudal epidural injections in discogenic or axial pain without disc herniation, radiculitis, facet joint pain, or sacroiliac joint pain.

2.6.3 Spinal Stenosis

Available evidence is fair based on one long-term randomized trial (59,65) with positive results with local anesthetic with or without steroids.

Of the 2 observational studies evaluating long-term results (76,149), positive results were illustrated in only one study (149). However, the second study utilized limited injections in the beginning and evaluated the patients at the end of the year with 35% improvement, illustrating clinical positive results. The fair evidence was supported by these 2 non-randomized studies.

2.6.4 Post Surgery Syndrome

The evidence for post lumbar surgery syndrome was fair based on one high quality randomized double-blind trial (62,83) with one low quality randomized double-blind study (139). The third study (147), comparing local anesthetic with steroids and hypertonic sodium chloride solution and hyaluronidase, showed positive results for hyaluronidase which may only indicate emerging evidence.

2.6.5 Summary of Evidence

In summary, the evidence is good for radiculitis secondary to disc herniation with local anesthetics and steroids, fair with local anesthetic only, whereas it was fair for radiculitis secondary to spinal stenosis with local anesthetic and steroids, for axial pain without disc herniation, and post surgery syndrome with local anesthetic with or without steroids.

3.0 Complications

Complications related to caudal epidural injections are rare. However, occasional complications may become worrisome. The common complications are related to either the needle placement or related to the drug activity. These include infection, either local or epidural, abscess, discitis; intravascular injection either intervenous or intraarterial with hematoma formation, spinal cord infarction; extra epidural placement with subcutaneous injection; subdural injection, dural puncture with post lumbar puncture headache, nerve damage, intracranial air injection or increased intracranial pressure; pulmonary embolism; and adverse effects of steroids (1,14,20,28,30,46-54,59-65,67-89,118-120,202-219).

Botwin et al (52) reported complications of fluoroscopically guided caudal epidural injections in 139 patients, who received 257 injections. Complications per injection included insomnia the night of the injection (4.7%), transient non-positional headaches (3.5%), increased back pain (3.1%), facial flushing (2.3%), vasovagal reactions (0.8%), nausea (0.8%), and increased leg pain (0.4%). The incidence of minor complications was 15.6% per injection.

Manchikanti et al (46) reported complications with pain during the injection with back pain in 43% of the patients and leg pain in 22% of the patients. They also noted postoperative complications in 34% of the patients with soreness at the injection site in 18%, increased pain in 5%, muscle spasms in 4%, swelling in 4%, headache in 3%, minor bleeding in 2%, dizziness in 1%, nausea and vomiting in 1%, fever in 1%, numbness in 1%, and voiding difficulty in 1%. Manchikanti et al (46,47) reported with fluoroscopically guided caudal epidural injections intravascular placement in 14% of the patients. They also reported complications in 7% of the patients with soreness at the injection site in 6%, increased pain in 1%, muscle spasms in 1%, headache in 1%, and nausea and vomiting in 1%.

Other much less common complications include transient blindness (202), retinal hemorrhage and necrosis (203,204), serous chorioretinopathy (205,206), persistent recurrent intractable hiccups (207), flush-

ing (208,209), chemical meningitis (210), arachnoiditis (211), discitis (212), epidural hematoma (213), epidural abscess (214), and other complications.

Other complications of corticosteroid administration include suppression of pituitary-adrenal axis, hypercorticism, Cushing's syndrome, osteoporosis, avascular necrosis of bone, steroid myopathy, epidural lipomatosis, weight gain, fluid retention, and hyperglycemia (216-219). The most commonly used steroids in neural blockade in the United States, methylprednisolone acetate, triamcinolone acetonide, betamethasone acetate, and phosphate mixture, have all been shown to be safe at epidural therapeutic doses in both clinical and experimental studies (219-229). The radiation exposure is also a potential problem with damage to eyes, skin, and gonads (230). However, some publications have shown a lack of effect on weight (46-54,59-65,67-89,118-120,231,232).

4.0 Discussion

This systematic review evaluating the effectiveness of caudal epidural injections in managing chronic low back and lower extremity pain caused by disc herniation with radiculitis showed good evidence for caudal epidural injections. However, the evidence is fair for spinal stenosis, axial pain, and post surgery syndrome. This evidence is superior when compared to lumbar interlaminar epidural injections and lumbar transforaminal epidural injections, specifically in reference to spinal stenosis and post surgery syndrome (233,234). In this evaluation, a total of 11 randomized trials and 5 non-randomized studies were included. Only the studies meeting at least moderate quality criteria were included in analysis. The quality assessment of all the manuscripts was performed. This review yielded similar results to Conn et al (28) published in 2009, critical review of APS guidelines (32), and reassessment of the American College of Occupational and Environmental Medicine (ACOEM) guidelines (50). However, these results do not correlate with results by Chou and Huffman (20) and Staal et al (14,108). Further, results provided by other reviewers are also in line with the evidence from this review (71,72,235).

Peterson and Hodler (71) in their evaluation of evidence-based radiology, evaluating the evidence for use of therapeutic injections for the spine and sacroiliac joints, concluded that caudal epidural steroid injections were superior. Further, the guidelines for the American Society of Anesthesiologists (ASA) and the American Society of Regional Anesthesia in Pain Medicine (ASRA) also provided favorable evidence.

However, Chou and Huffman (20), Staal et al (14,108), ACOEM guidelines (50), and guidelines from American Academy of Neurology (AAN) (236) provided different conclusions. Chou and Huffman (20) in their evaluation, stated that most placebo-controlled trials evaluated either the interlaminar or caudal approach. They combined interlaminar or translaminar epidural injections and caudal epidural injections into one category, and therefore reached erroneous conclusions that these treatments were only effective for short-term relief in radiculopathy.

Staal et al (14,108) evaluated all epidural injections in combination which included caudal, lumbar interlaminar, and lumbar transforaminal as one category. They also failed to separate the response to herniation, stenosis, post laminectomy syndrome, or discogenic pain, consequently reaching inappropriate conclusions. Thus, the present systematic review contradicts this evidence.

The ASA and ASRA guidelines (235) utilizing a combined approach with physician consensus and systematic review, also recommend epidural steroid injections.

The current systematic review shows that caudal epidural steroid injections, when appropriately performed, should result in significant improvement in pain and function.

The debate concerning caudal epidural steroid injections has been nurtured since the 1970s (1,14,20,30,48-50,108,233-240). The first systematic review of the effectiveness of caudal epidural steroid injections was performed by Kepes and Duncalf in 1985 (238). They concluded that the rationale for epidural and systematic steroids was not proven, however, in 1986, Benzon (239), utilizing the same studies, concluded that mechanical causes of low back pain, especially those accompanied by signs of nerve root irritation, may respond to epidural steroid injections. Thus, this illustrates that systematic reviews have provided different results based on the evaluators.

Bogduk et al (30) extensively studied caudal, interlaminar, and transforaminal epidural injections, including all the literature available at the time, and concluded that the balance of published evidence supports the therapeutic use of caudal epidurals. In 1995, Koes et al (237) reviewed 12 trials of lumbar and caudal epidural steroid injections and reported positive results from only 6 studies. However, review of their analysis showed that there were 5 studies for caudal epidural steroid injections and 7 studies for lumbar epidural steroid injections. However, 4 of the 5 studies involving caudal

epidural steroid injections were positive, whereas 5 of 7 studies for lumbar interlaminar were negative. Their updated analysis (240) with the inclusion of 15 trials also arrived at the same conclusions with inappropriate allocation of the procedures. Multiple other investigators (108,236,237) also have provided differing conclusions. In general, criticism against systematic reviews in the past has been directed toward methodology, small size of the study populations, and other limitations, including long-term follow-up and outcome parameters of the available literature. Further, the paucity of literature has been a factor in the systematic evaluation of evidence for the effectiveness of epidural injections.

This systematic review provides information that caudal epidural injections are effective and there may not be any significant difference with the addition of steroids when appropriately performed with steroids and fluoroscopy.

Placebo-controlled neural blockade is not realistic even though it has been misinterpreted as most placebo solutions injected into active structures result in active effects (185-198). The underlying mechanism of action of epidurally administered steroid and local anesthetic injection is still not well understood. It is believed that the achieved neural blockade alters or interrupts nociceptive input, the reflex mechanism of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities (1,219). Further, corticosteroids have been shown to reduce inflammation by inhibiting either the synthesis or release of a number of proinflammatory mediators and by causing a reversible local anesthetic effect (241-245). Local anesthetics also have been described to provide short- to long-term symptomatic relief based on alteration of various mechanisms including excess nociceptive process, excess release of neurotransmitters, nociceptive sensitization of the nervous system, and phenotype changes (244-251). The prolonged effect of local anesthetics in epidural injections and facet joint nerve blocks has been demonstrated in a multiple of studies (62-65,81,89,118-124,250). Sato et al (201) evaluated the prolonged analgesic effect of epidural bupivacaine in a rat model of neuropathic pain with repetitive administration, possibly by inducing a plastic change in nociceptive input. Further, Tachihara et al (200) showed in rats that nerve root infiltration prevented mechanical allodynia; however, no additional benefit from using corticosteroid was identified.

Further discussions with regards to the superiority of caudal epidurals over either transforaminal epidural injections or interlaminar epidural injections is not proven by this systematic review. This systematic review however shows the ability of caudal epidural injections to prevent surgical interventions.

The results of this systematic review may be applied in interventional pain management practices utilizing appropriate evaluations (64). In this systematic review, mostly active control trials or practical clinical trials were utilized. Practical clinical trials measure effectiveness. Consequently, these are considered more appropriate than explanatory trials meeting efficacy (96,97,252-256). The differences between placebo-control trials and active control trials include the fact that placebo control trials measure absolute effect size and show the existence of the effect, whereas active control trials, not only show the existence of effect, but compared the therapies (257). Thus, the results of this systematic review may be considered generalizable if appropriate selection criteria are utilized.

The limitations of this study include that we were able to find only 16 appropriately performed studies which met inclusion criteria and were clinically relevant. Further, methodological criteria has been highly variable along with sample sizes. The studies were heterogenous. The results of this systematic review have significant implications for clinical practice. Caudal epidural injections show a significant reduction in pain scores of patients with lumbar radiculitis, axial low back pain, spinal stenosis, and post surgery syndrome when compared to doing nothing, and conservative management without injection therapy.

5.0 Conclusion

The results of this systematic review evaluating the effect of caudal epidural injections with or without steroids in managing various types of chronic low back and lower extremity pain emanating as a result of disc herniation or radiculitis, post lumbar laminectomy syndrome, spinal stenosis, and chronic discogenic pain without disc herniation or radiculitis has shown good evidence for short- and long-term relief of chronic pain secondary to disc herniation or radiculitis with local anesthetic and steroids and fair relief with local anesthetic only. Further, this systematic review also provided indicated evidence of fair for caudal epidural injections in managing chronic axial or discogenic pain, spinal stenosis, and post surgery syndrome. The results of this systematic review are provided utilizing contemporary systematic review methodology utilizing randomized trials and observational studies, even though most of the evidence was derived from randomized trials.

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