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Systematic Review

Systematic Review of the Effectiveness of Cervical Epidurals in the Management of Chronic Neck Pain

Ramsin Benyamin, MD[1], Vijay Singh, MD[2], Allan T. Parr, MD[3], Ann Conn, MD[4], Sudhir Diwan, MD[5], and Salahadin Abdi, MD, PhD[6]

From: [1]Millennium Pain Center, Bloomington, IL; [2]Pain Diagnosic Associates, Niagara WI; [3-4]Premier Pain Center, Covington, LA; [5]New York Presbyterian Hospital, Weill Cornell Medical College New York, NY; and [6]University of Miami, Miller School of Medicine, Miami, FL

Dr. Benyamin is Medical Director, Millennium Pain Center, Bloomington IL; and Clinical Instructor, Department of Surgery, College of Medicine, University of Illinois, Urbana-Champaign, IL.
Dr. Singh is Medical Director, Pain Diagnostic Associates, Niagara, WI .
Dr. Parr is Medical Director, Premier Pain Center, Covington, LA
Dr. Conn is staff physician, Premier Pain Relief, Covington, LA
Dr. Diwan is Director of Pain Medicine in the Department of Anesthesiology, New York Presbyterian Hospital, the Director of the Tri-Institutional Pain Fellowship Program, Weill Cornell Medical College, New York, NY
Dr. Abdi is Professor and Chief, Division of Pain Medicine, Department of Anesthesiology, Perioperative Medicine and Pain Management, University of Miami, Miller School of Medicine, Miami, FL

Address correspondence:
Ramsin Benyamin, MD
Medical Director
Millennium Pain Center
1015 S. Mercer
Bloomington IL 61701
E-mail:
ramsinbenyamin@yahoo.com

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Background: Chronic neck pain is a common problem in the adult population with a typical 12-month prevalence of 30% to 50%, and 14% of the patients reporting grade II to IV neck pain with high pain intensity and disability that has a substantial impact on health care and society.

Cervical epidural injections for managing chronic neck pain are one of the commonly performed interventions in the United States. However, the literature supporting cervical epidural steroids in managing chronic pain problems has been scant and no systematic review dedicated to the evaluation of cervical interlaminar epidurals has been performed in the past.

Study Design: A systematic review of cervical interlaminar epidural injections.

Objective: To evaluate the effect of cervical interlaminar epidural injections in managing various types of chronic neck and upper extremity pain emanating as a result of cervical spine pathology.

Methods: The available literature of cervical interlaminar epidural injections in managing chronic neck and upper extremity pain was reviewed. The quality assessment and clinical relevance criteria utilized were the Cochrane Musculoskeletal Review Group criteria as utilized for interventional techniques for randomized trials and the criteria developed by the Agency for Healthcare Research and Quality (AHRQ) criteria for observational studies.

The level of evidence was classified as Level I, II, or III based on the quality of evidence developed by the U.S. Preventive Services Task Force (USPSTF) for therapeutic interventions.

Data sources included relevant literature of the English language identified through searches of PubMed and EMBASE from 1966 to November 2008, and manual searches of bibliographies of known primary and review articles.

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

Results: The indicated evidence is Level II-1 in managing chronic neck and upper extremity pain.

Limitations: The limitations of this systematic review include the paucity of literature and lack of randomized trials performed under fluoroscopy.

Conclusion: The results of this systematic evaluation of cervical interlaminar epidural injection showed significant effect in relieving chronic intractable pain of cervical origin and also providing long-term relief with an indicated evidence level of Level II-1.

Key words: Cervical disc herniation, cervical post surgery syndrome, cervical spinal stenosis, cervical radiculitis, cervical interlaminar epidural injections, local anesthetic steroids, chronic discogenic pain

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Neck pain is common in the adult general population, disabling and costly (1-9). Lifetime prevalence of neck pain has been reported to be 26% to 71% with 12-month prevalence estimates ranging from 30% to 50% (1,4). Studies of the prevalence of chronic neck pain (2-9) and its impact on general health (3,8,10) showed 14% of patients reporting Grade II to IV neck pain with high pain intensity with disability. Similar to low back pain, neck pain is also associated with significant economic, societal, and health impact, though not to the same extent as low back pain. In fact, neck pain has been well recognized as a source of disability in the working population (11-15). Neck pain has been reported to account for approximately 15% of hospital physiotherapy and 30% of chiropractic visits (4). In addition, industrial neck-related disorders may cause absenteeism as commonly as low back pain (4,11-14). In Quebec, it was reported that 7% of compensation claims were neck-related (16). In addition, motor vehicle injuries result in 24% to 50% of those involved with persistent symptoms at 12 months (17,18).

Multiple structures causing neck and upper extremity pain and headache include cervical intervertebral disc, cervical facet joints, atlanto-axial and atlanto-occipital joints, ligaments, fascia, muscles, and nerve root dura which are capable of transmitting pain. However, very little is known about the causes of neck pain. The epidemiologic studies do not reveal either the source or the cause of pain. Bogduk (19) postulated the requirements for a structure to be deemed a cause of back pain to include the nerve supply, capability of causing pain similar to that seen clinically, ideally demonstrated in normal volunteers, susceptibility to diseases or injuries that are known to be painful, and shown to be a source of pain in patients using diagnostic techniques of known reliability and validity. Lotz and Ulrich (20) described that symptoms derived from a degenerated disc may be classified into 2 types: type 1, radicular pain secondary to stenosis and nerve root, and, type 2, discogenic pain due to internal disc disruption. Yin and Bogduk (21) attempted to determine the prevalence of different causes of neck pain in a private practice clinic in the United States using multiple denominators. While a large proportion of patients with chronic neck pain (36%) did not pursue investigations and 17% deferred completing investigations, among the 46% (143 patients) who completed the investigations, the prevalence of discogenic pain was 16%, zygapophysial joint pain was 55%, and lateral atlanto-axial joint pain was 9%. Consequently, a diagnosis remained elusive in 32% of those patients who completed the investigations. Bogduk and Aprill (22) investigated the prevalence of zygapophysial and discogenic pain and the results showed discogenic pain without zygapophysial joint pain in 20% of the sample, whereas both a symptomatic disc and a symptomatic zygapophysial joint were identified in the same segment in 41% of the patients. Thus, based on controlled diagnostic blocks, cervical facet joints have been implicated as being responsible for pain in the neck, head, and upper extremities in 36% to 67% of patients (21,23-30), whereas reports of cervical discogenic pain (21,22) show a prevalence of 16% to 20%. Further, Yin and Bogduk (21) reported that of the 143 patients with chronic neck pain, only 5 patients were diagnosed with cervical radicular pain on the basis of history and clinical examination, while the remaining patients had idiopathic neck pain. It has been shown that by far the most common causes of cervical radiculopathy are disc protrusion and cervical spondylosis. The mechanism of cervical radicular pain continues to be an enigma with scant literature. However, based on the experience in the lumbar spine, it appears that cervical radicular pain may be caused by mechanical compression, nerve root irritation, and/or neurotoxicity (31-47).

Epidural injections for managing chronic neck pain are one of the commonly performed interventions in the United States (4,48-54). Cervical epidural injections have been used to treat radicular pain from herniated discs, spinal stenosis, chemical discs, chronic pain secondary to post-cervical surgery syndrome, and chronic neck pain of discogenic origin. Epidural injections in the cervical spine are performed either by interlaminar or transforaminal approaches. There has been one systematic review (53), multiple guidelines (2), a Cochrane review of medicinal and injection therapies for mechanical neck disorders (4), and a document reassessing the evidence of the American College of Occupational and Environmental Medicine (ACOEM) guidelines (54) that included analysis of cervical epidural injections. However, the evidence for cervical interlaminar epidural injections has been a subject of debate and at best has had only moderate in success managing cervical radiculopathy, while there is no evidence available in the management of axial neck pain, post-surgery syndrome, or discogenic pain.

The purpose of this systematic review is to evaluate cervical epidural injections with or without steroids in the management of chronic neck pain and upper extremity pain.

Methods

Literature Search

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

The search strategy emphasized chronic neck pain of discogenic origin with a focus on cervical epidural injections. Search terminology included cervical intervertebral disc, disc-related pain, spinal stenosis, post surgery syndrome, and cervical epidural injections.

Selection Criteria

The review focused on randomized trials and observational studies and reports of complications. The population of interest was patients suffering with chronic mechanical or whiplash-related neck pain with or without radicular findings for at least 3 months. Only cervical epidural injections with or without steroids were evaluated. All the studies providing appropriate management with outcome evaluations of 6 months or longer and statistical evaluations were reviewed. Reports without appropriate diagnosis, non-systematic reviews, book chapters, and case reports were excluded.

Outcome Parameters

The outcome measures were of documented pain relief at various points in time, functional assessment, and other outcomes including psychological improvement, return to work, and change in opioid intake.

Review Criteria

Each study was evaluated by 2 physicians for stated criteria and any disagreements were resolved by a third physician.

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, clinical relevance, evidence synthesis, or grading of evidence.

Methodologic Quality Assessment

The quality of each individual article used in this analysis was assessed by modified Cochrane review criteria with weighted scores (Table 1) (55) for randomized trials and the Agency for Healthcare Research and Quality (AHRQ) quality criteria for assessment of observational studies (Table 2) (56) with consensus-based weighted scoring developed by the guidelines' committee of the American Society of Interventional Pain Physicians (ASIPP) utilized in other evaluations (54,57-60).

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

Clinical Relevance

Clinical relevance of the included studies was evaluated according to 5 questions recommended by the Cochrane Back Review Group (61,62).

Table 3 shows the clinical relevance questions. Each question was scored positive (+) if the clinical relevance item was met, negative (–) if the item was not met, and unclear (?) if data were not available to answer the question.

In the recent Cochrane review of "Injection Therapy for Subacute and Chronic Low Back Pain" (62) the authors considered a 20% improvement in pain scores (63) and a 10% improvement in functioning outcomes (64) to be clinically important. This study utilized stricter criteria than general systematic reviews and previous systematic reviews. Any relief of 6 months or less was considered as short-term, whereas Cochrane reviews (62) and others have considered 6 weeks as short-term and longer than 6 weeks as long-term. We also utilized methodologic quality assessment criteria (62) for minimum inclusion, thus this systematic review is expected to provide robust results with stricter criteria. However, in contrast to many other systematic reviews, we have not excluded observational studies and included only quality observational studies with scores of 50 or more on a scale of 0 - 100 based on AHRQ criteria. This improves the generalizability of the systematic review as well as the intervention (65-68).

Analysis of Evidence

Analysis was conducted using 5 levels of evidence, ranging from Level I to III with 3 subcategories in Level II, as illustrated in Table 4 (69).

Table 1. *Modified and weighted Cochrane methodologic quality assessment criteria.*

CRITERION		Weighted Score (points)
1. Study population		**35**
A	Homogeneity	2
B	Comparability of relevant baseline characteristics	5
C	Randomization procedure adequate	4
D	Drop-outs described for each study group separately	3
E	< 20% loss for follow-up	2
	< 10% loss for follow-up	2
F	> 50 subject in the smallest group	8
	> 100 subjects in the smallest group	9
2. Interventions		**25**
G	Interventions included in protocol and described	10
H	Pragmatic study	5
I	Co-interventions avoided or similar	5
J	Placebo-controlled	5
3. Effect		**30**
K	Patients blinded	5
L	Outcome measures relevant	10
M	Blinded outcome assessments	10
N	Follow-up period adequate	5
4. Data-presentation and analysis		**10**
O	Intention-to-treat analysis	5
P	Frequencies of most important outcomes presented for each treatment group	5
	TOTAL SCORE	100

Adapted from Koes BW et al. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. Pain 1995; 63:279-288 (55).

Recommendations

Grading recommendations were based on Guyatt et al's criteria as illustrated in Table 5 (70).

Outcome of the Studies

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

For observational studies, a study was judged to be positive if the epidural injection therapy was effective, with outcomes reported at the reference point with positive or negative results at 3 months, 6 months, and one year. Relief of 6 months or less was considered as short-term and relief of longer than 6 months was considered as long-term.

Studies performed under fluoroscopy were given priority.

Results

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

Our search strategy yielded multiple studies evaluating the effectiveness of cervical interlaminar epidural injections with or without steroids (71-90). These included 3 randomized or double-blind trials (71,74,85), and 17 observational studies (72,73,75-84,86-90).

Table 2. *Modified AHRQ quality assessment criteria for observational studies.*

CRITERION	Weighted Score (points)
1. Study Question	2
• Clearly focused and appropriate question	
2. Study Population	8
• Description of study population	5
• Sample size justification	3
3. Comparability of Subjects	22
• Specific inclusion/exclusion criteria for all groups	5
• Criteria applied equally to all groups	3
• Comparability of groups at baseline with regard to disease status and prognostic factors	3
• Study groups comparable to non-participants with regard to confounding factors	3
• Use of concurrent controls	5
• Comparability of follow-up among groups at each assessment	3
4. Exposure or Intervention	11
• Clear definition of exposure	5
• Measurement method standard, valid and reliable	3
• Exposure measured equally in all study groups	3
5. Outcome measures	20
• Primary/secondary outcomes clearly defined	5
• Outcomes assessed blind to exposure or intervention	5
• Method of outcome assessment standard, valid and reliable	5
• Length of follow-up adequate for question	5
6. Statistical Analysis	19
• Statistical tests appropriate	5
• Multiple comparisons taken into consideration	3
• Modeling and multivariate techniques appropriate	2
• Power calculation provided	2
• Assessment of confounding	5
• Dose-response assessment if appropriate	2
7. Results	8
• Measure of effect for outcomes and appropriate measure of precision	5
• Adequacy of follow-up for each study group	3
8. Discussion	5
• Conclusions supported by results with possible biases and limitations taken into consideration	
9. Funding or Sponsorship	5
• Type and sources of support for study	
TOTAL SCORE	**100**

Adapted and modified from West S et al. Systems to Rate the Strength of Scientific Evidence, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016 (56).

Table 3. *Clinical relevance questions*.

A)	Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?
B)	Are the interventions and treatment settings described well enough so that you can provide the same for your patients?
C)	Were all clinically relevant outcomes measured and reported?
D)	Is the size of the effect clinically important?
E)	Are the likely treatment benefits worth the potential harms?

Source: Staal JB et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (62).

Table 4. *Quality of evidence developed by USPSTF.*

I:	**Evidence obtained from at least one properly randomized controlled trial**
II-1:	**Evidence obtained from well-designed controlled trials without randomization**
II-2:	**Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group**
II-3:	**Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence**
III:	**Opinions of respected authorities, based on clinical experience descriptive studies and case reports or reports of expert committees**

Adapted from the U.S. Preventive Services Task Force (USPSTF) (69).

Table 5. *Grading recommendations*.

Grade of Recommendation/ Description	Benefit vs Risk and Burdens	Methodological Quality of Supporting Evidence	Implications
1A/strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1B/strong recommendation, moderate quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
1C/strong recommendation, low-quality or very low-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
2A/weak recommendation, high-quality evidence	Benefits closely balanced with risks and burden	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2B/weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burden	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
2C/weak recommendation, low-quality or very low-quality evidence	Uncertainty in the estimates of benefits, risks, and burden; benefits, risk, and burden may be closely balanced	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

Adapted from Guyatt G et al. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians task force. *Chest* 2006; 129:174-181 (70).

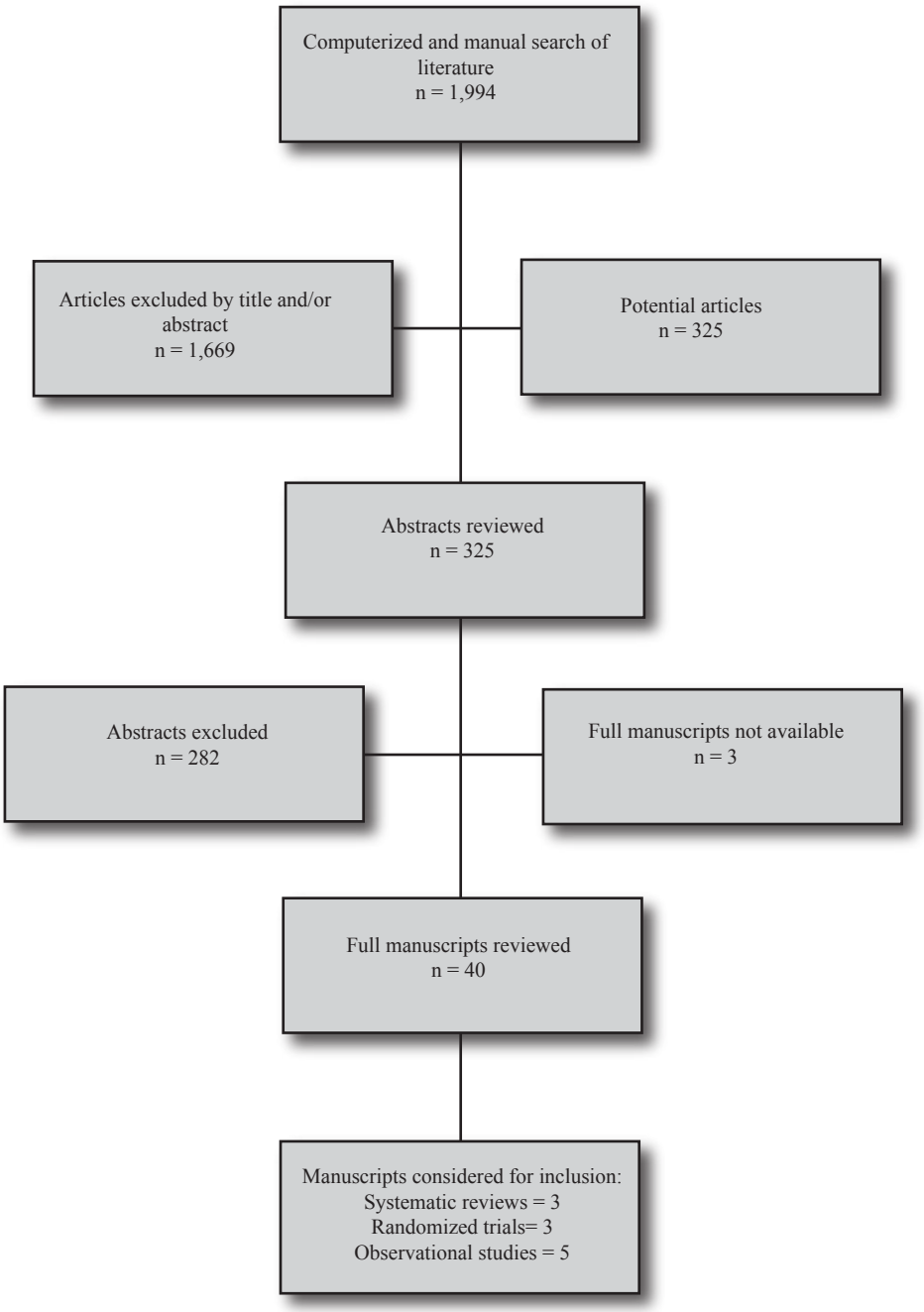

Fig. 1. *The flow diagram illustrating randomized trials, observational studies, and systematic reviews evaluating caudal epidural injections.*

Methodologic Quality Assessment

Of the randomized trials, all 3 studies met the inclusion criteria (71,74,85) for methodological assessment and clinical relevance. Among observational studies, 5 met the inclusion criteria (76,79,80,82,89). Methodologic quality assessment criteria and clinical relevance criteria for randomized trials are illustrated in Tables 6 and 7, whereas methodologic quality criteria for observational studies are illustrated in Table 8.

The quality assessment criteria ranged from 50 to 56 with all 3 randomized trials eligible to be included in the analysis. The clinical relevance criteria as illustrated in Table 7 showed clinical relevance for all 3 randomized trials.

The quality assessment criteria for observational studies is illustrated in Table 8. From a total of 10 ob-

Table 6. *Methodological assessment of randomized clinical trials evaluating the effectiveness of cervical interlaminar epidural injections.*

CRITERION		WEIGHTED SCORE (points)	Castagnera et al (74)	Stav et al (71)	Pasqualucci et al (85)
Study population					
A	Homogeneity	2	2	2	2
B	Comparability of relevant baseline characteristics	5	5	5	5
C	Randomization procedure adequate	4	2	2	4
D	Drop-outs described for each study group separately	3	3	3	3
E	< 20% loss for follow-up	2	2	__	2
	< 10% loss for follow-up	2	2	__	__
F	> 50 subject in the smallest group	8	__	__	__
	> 100 subjects in the smallest group	9	__	__	__
Interventions					
G	Interventions included in protocol and described	10	10	10	10
H	Pragmatic study	5	5	__	5
I	Co-interventions avoided or similar	5	__	5	5
J	Placebo-controlled	5	__	5	__
Effect					
K	Patients blinded	5	5	__	__
L	Outcome measures relevant	10	4	8	6
M	Blinded outcome assessments	10	__	__	6
N	Follow-up period adequate	5	5	5	3
Data-presentation and analysis					
O	Intention-to-treat analysis	5	5	__	__
P	Frequencies of most important outcomes presented for each treatment group	5	5	5	5
	TOTAL SCORE	100	55	50	56

Methodological criteria and scoring adapted from Koes BW et al. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. *Pain* 1995; 63:279-288 (55).

Table 7. *Clinical relevance of randomized clinical trials evaluating the effectiveness of cervical interlaminar epidural injections.*

	Castagnera et al (74)	Stav et al (71)	Pasqualucci et al (85)
A) Are the patients described in detail so that you can decide whether they are comparable to those that you see in your practice?	+	+	+
B) Are the interventions and treatment settings described well enough so that you can provide the same for your patients?	+	+	-
C) Were all clinically relevant outcomes measured and reported?	+	+	+
D) Is the size of the effect clinically important?	+	+	+
E) Are the likely treatment benefits worth the potential harms?	+	+	-
TOTAL CRITERIA MET	5/5	5/5	3/5

+ = positive; - = negative
Scoring adapted from Staal JB et al. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824 (62).

servational studies available, 5 of them met inclusion criteria for methodologic quality assessment. Studies excluded from methodologic quality assessment were as follows: full manuscripts were not available for review of Mangar and Thomas (81), Catchlove and Braha (84), and Martelletti et al (88). Martelletti et al (87), in another manuscript, evaluated short-term relief for management of cervicogenic headache in 9 patients. Kwon et al (86) attempted to verify the usefulness of fluoroscopically guided cervical interlaminar epidural steroid injections in patients with neck pain and cervical radiculopathy. Of the 4 studies meeting the quality assessment criteria for observational studies, the scores ranged from 28 to 48 with none of them meeting criteria for inclusion in the evidence synthesis.

Clinical Relevance Assessment

All 3 studies met clinical relevance criteria (71,74,85).

Study Characteristics

Study characteristics of randomized trials of cervical interlaminar epidural injections are illustrated in Table 9.

Castagnera et al (74) randomly allocated 24 patients into 2 groups with the steroid group treated with 0.5% lidocaine plus triamcinolone acetonide 10 mg/mL, whereas the morphine group received the same combination of 0.5% lidocaine and steroid plus 2.5% of morphine. Pain relief was assessed as the percentage of pain decrease on a visual analog scale (VAS) at months 3, 6, 8, and 12 after cervical epidural steroid injection, up to 48 months. They reported a success rate of 78.5% in the steroid group and 80% in the steroid and morphine group with pain relief which was stable, and a mean follow-up of 43 + 18.1 months.

This is a well performed study; however, the authors attempted to evaluate the pain by increasing the volume of sodium chloride solution injection into the cervical epidural space, not to exceed 10 mL to exacerbate the patient's radicular pain. The mean volume injected in the epidural space was 6.6 + 2.1 and 6.3 + 1.9 mL in the respective groups. This report however showed results much more superior to any other study reported in the literature. They also showed that pain relief remained stable for 48 months and in some cases for more than 60 months. The intensity of medical treatment also decreased significantly 3 months after cervical epidural steroid injection and remained unchanged over subsequent periods. They also showed return to work in all the patients who were working prior to the cervical epidural steroid injections. However, there was no correlation found between pain relief and absenteeism. Further, the use of morphine has not been shown to be superior in this study. Even though significant differences were observed, this study was limited by the small sample sizes of 14 and 10 in the 2 groups.

Stav et al (71) treated 25 patients with epidural steroid and lidocaine injections and 17 patients with steroid and lidocaine injections into the posterior neck muscles. They administered 1 to 3 injections at 2 week intervals based on the clinical response. Pain relief was evaluated by the VAS one week after the last injection and then one year later. One week after the last injection, good pain relief was reported in 76% of the pa-

Table 8. *Illustration of methodologic assessment of observational studies of cervical interlaminar epidural injections.*

CRITERION	Weighted Score (points)	Rowlingson & Kirschenbaum (76)	Ferrante et al (82)	Grenier et al (89)	Proana et al (80)	Cicala et al (79)
1. Study Question	2	2	2	2	2	2
• Clearly focused and appropriate question		2	2	2	2	2
2. Study Population	8	5	5	5	5	5
• Description of study population	5	5	5	5	5	5
• Sample size justification	3	__	__	__	__	__
3. Comparability of Subjects for All Observational Studies	22	3	3	3	3	8
• Specific inclusion/exclusion criteria for all groups	5	3	3	3	3	5
• Criteria applied equally to all groups	3	__	__	__	__	3
• Comparability of groups at baseline with regard to disease status and prognostic factors	3	__	__	__	__	__
• Study groups comparable to non-participants with regard to confounding factors	3	__	__	__	__	__
• Use of concurrent controls	5	__	__	__	__	__
• Comparability of follow-up among groups at each assessment	3	__	__	__	__	__
4. Exposure or Intervention	11	5	5	5	5	5
• Clear definition of exposure	5	5	5	5	5	5
• Measurement method standard, valid and reliable	3	__	__	__	__	__
• Exposure measured equally in all study groups	3	__	__	__	__	__
5. Outcome measures	20	3	8	10	10	10
• Primary/secondary outcomes clearly defined	5	__	3	5	5	5
• Outcomes assessed blind to exposure or intervention	5	__	__	__	__	__
• Method of outcome assessment standard, valid and reliable	5	__	__	__	__	__
• Length of follow-up adequate for question	5	3	5	5	5	5
6. Statistical Analysis	19	__	10	__	__	8
• Statistical tests appropriate	5	__	5	__	__	5
• Multiple comparisons taken into consideration	3	__	3	__	__	3
• Modeling and multivariate techniques appropriate	2	__	2	__	__	__
• Power calculation provided	2	__	__	__	__	__
• Assessment of confounding	5	__	__	__	__	__
• Dose-response assessment if appropriate	2	__	__	__	__	__
7. Results	8	__	5	5	5	5
• Measure of effect for outcomes and appropriate measure of precision	5	__	3	3	3	3
• Adequacy of follow-up for each study group	3	__	2	2	2	2
8. Discussion	5	5	5	5	5	5
• Conclusions supported by results with possible biases and limitations taken into consideration						
9. Funding or Sponsorship	5	5	5	5	5	5
• Type and sources of support for study						
TOTAL SCORE	100	28	48	40	40	48

Adapted and modified from West S et al. Systems to Rate the Strength of Scientific Evidence, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016 (56).

Table 9. *Characteristics of randomized trials of cervical interlaminar epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief ≤6 months Long-term relief > 6 months
Castagnera et al (74) 1994 Randomized trial	14 patients: local anesthetic and steroid. 10 patients: local anesthetic, steroid + morphine sulfate.	I. 0.5% lidocaine + triamcinolone acetonide. II. Local anesthetic + steroid + 2.5 mg of morphine sulfate.	Timing: 1 month, 3 mos, and 12 mos. Outcome measures: pain relief.	The success rate was 79% vs. 80% in group I and II. Overall, initial success rate was 96%, 75% at 1 month, 79% at 3 mos, 6 mos, and 12 mos.	Positive short-term and long-term relief
Stav et al (71) 1993 Randomized trial	Experimental: 25 patients. Control: 17 patients.	Experimental: epidural steroid and lidocaine injections. Control: steroid and lidocaine injections into the posterior neck muscles.	Timing: 1 week and 1 year. Outcome measures: pain relief, change in range of motion, reduction of daily dose of analgesics, return to work.	One week improvement 36% vs 76%; One year improvement 12% vs 68%.	Positive short-term and long-term relief
Pasqualucci et al (85) 2007 Randomized trial	Single = 20 Continuous=20 Over 180 days Patients were divided into 4 groups, 40 patients per group on the basis of the time, pain, onset. Group A: 40 patients with pain onset 15-30 days. Group B: 40 patients with pain from 31 to 60 days. Group C: 40 patients with pain from 61 to 180 days. Group D: 40 patients with pain more than 180 days.	Patients of each group were randomized based on received therapy: 20 with single injection and 20 with continuous epidural. Patients in the single injection group were administered a series of epidural blocks every 4 to 5 days with bupivacaine 6 mL and methylprednisolone 80 mg. The second block, after 4 to 5 days, was done with 6 mL of methylprednisolone acetate with the second block 4 to 5 days later, with the third block also 4 to 5 days. Treatment was continued if pain relief was less than 80% with a maximum of 9 blocks.	Timing: 1 month and 6 months. Outcome measures: pain control > 80%, number of pain-free hours of sleep.	The duration of the 3 therapies increased with the increase in pain chronicity. Statistically significant efficacy of the treatment of cervicobrachial pain with epidural local anesthetic plus corticosteroids was demonstrated with continuous infusion rather than with single injection, in patients with chronic pain who did not respond to conservative therapies (patients with 180 days or longer). There was no significant difference between the 2 treatments in patients with pain less than 180 days.	Positive short-term relief. Results of long-term relief are not available in chronic pain patients with duration of chronic pain of 180 days or longer.

tients receiving epidural steroids and local anesthetic as compared to 35.5% of the patients receiving extra-epidural steroids and local anesthetic. One year after the treatment, 68% of the patients in the epidural steroid group still had very good pain relief, whereas only 11.8% of the patients receiving intramuscular or extra-epidural with local anesthetic reported good pain relief. The study also reported that patients were able to increase range of motion, a few of them reduced their daily dose of analgesics, and recovery of the capacity for work was significantly better in the epidural steroid group.

The disadvantages of this study include lack of fluoroscopic visualization, epidural entry at multiple levels with some between C4 and C5, and lack of patient blinding with administration of intramuscular steroid lidocaine injection.

Pasqualucci et al (85) evaluated the efficacy of

epidural local anesthetics plus steroids for the treatment of cervicobrachial pain in 160 patients randomized based on the duration of the pain and administering 2 types of treatments with a maximum of 9 blocks of single injections or 30 days of continuous epidural with the achievement of pain control of 80% or greater. The enrolled 160 patients were divided in 4 groups with 40 patients per group on the basis of the time of pain onset with Group A with 40 patients with pain onset of 15 to 30 days; Group B with 40 patients with pain from 31 to 60 days; Group C with 40 patients with pain from 61 to 180 days; and Group D with 40 patients with pain of greater than 180 days. Patients of each group were randomized based on their received therapy with 20 in the single injection group and 20 with a continuous epidural.

Patients in the single injection group were administered a series of epidural blocks every 4 to 5 days with administration of 0.25% bupivacaine 6 mL, with 80 mg of methylprednisolone for a maximum of 9 blocks. In the continuous epidural group, catheterization was carried out and bupivacaine, a volume of 6 mL, combined with 80 mg of methylprednisolone was administered initially, followed by bupivacaine 6 mL every 6, 12, or 24 hours, along with methylprednisolone 40 mg every 4 to 5 days for a period of 30 days. They evaluated pain control and pain-free sleep status. Of the 160 enrolled patients, 19 were excluded due to various reasons. None of the patients had any major complications. The results of this evaluation showed a statistically significant efficacy of the treatment of cervicobrachial pain with epidural local anesthetic plus corticosteroids in continuous infusion rather than in single injection, in patients with chronic pain who did not respond to conservative therapies with pain duration of 6 months or longer. However, there was no statistically significant difference between the 2 treatments in patients with pain of less than 6 months. This data suggested that continuous epidural local anesthetic plus corticosteroid has greater efficacy than single injection of these drugs for the treatment of chronic cervicobrachial pain of greater than 6 months.

Although this study provides important information; it has several drawbacks: lack of long-term follow-up, lack of fluoroscopy, and inadequate blinding of patients and physicians.

Among the observational studies, Ferrante et al (82) in a retrospective analysis of 100 patients assessed potential predictors of outcome individually and then simultaneously with a multiple-recreation model. They concluded that patients with radicular symptoms and signs had the best pain relief and in contradiction to those with axial neck pain. The results showed that overall there was a 41% probability of a patient obtaining greater than 50% pain relief and at least a partial return to normal activities of daily living.

Rowlingson and Kirschenbaum (76) in a retrospective evaluation of 45 cervical epidural injections performed on 25 patients with cervical radiculopathy demonstrated that 64% of the patients had a good or excellent response to cervical epidural steroid injection, whereas other conservative modalities had not helped them. In contrast to Ferrante et al's study (82), in this evaluation, all patients had cervical radiculopathy and 64% (16 of 25) obtained a good or excellent response with full resumption of their daily activities and at least a 75% improvement in their pain complaints. Proano et al (80) in a review of charts from 1986 to 1989, with 176 cervical epidural injections on 61 patients, with a range of 1 to 6 blocks per patient, reported significant pain relief (greater than 50% reduction) in 62% of the patients, with 20% reporting complete relief of symptoms. Of the 61 patients, 20% went on to have surgery. Grenier et al (89) in an open prospective study evaluated the effect of a single epidural injection in patients suffering from non-compressive and non-surgical cervicobrachial neuralgia in 29 patients suffering for more than 12 months. After 3 months, a success rate of 83% was obtained. They also reported that pain relief remained stable for at least 24 months with a simultaneous decrease in controlled substances. Cicala et al (79) evaluated 58 patients over a 6-month period. Patients with 90% pain relief lasting 6 months were considered to have excellent results, those with greater than 50% relief lasting at least 6 months were considered to have good results, and all others were considered to have poor results. Six months after the injection, 41.4% or 24 patients showed excellent results, whereas 29.3% or 17 patients showed good results.

Effectiveness

Of the 3 randomized trials evaluating cervical interlaminar epidural steroid injections, all showed positive results for short-term relief (71,74,85), 2 were positive for long-term relief (71,74), and the results of long-term relief were not available for one study (85).

Table 10 illustrates results of effectiveness of cervical interlaminar epidural steroid injections.

Level of Evidence

The indicated evidence for cervical interlaminar epidural steroid injections is Level II-1 based on U.S. Preventive Services Task Force (USPSTF) criteria.

Recommendations

Based on Guyatt et al's criteria (70), the recommendation for cervical interlaminar epidurals is 1C/ strong recommendation. However, this recommendation may change when higher quality evidence becomes available.

Complications

The complications associated with interlaminar epidural steroid injections are few and usually minor (91-93). The most common and worrisome complications are of 2 types relating to the needle placement and drug administration and include subarachnoid entry, subdural entry, spinal cord trauma, infection, hematoma formation, abscess formation, intracranial air injection, epidural lipomatosus, nerve damage, headache, brain damage, increased intracranial pressure, intravascular injection, vascular injury, cerebrovascular or pulmonary embolus, death, and multiple effects of steroids (2,53,91-93). In the cervical spine specifically, complications include spinal cord trauma, spinal cord or epidural hematoma formation, subarachnoid or subdural injections, intravascular injection, vascular injury or vascular embolism, or catastrophic complications.

Botwin et al (91) reported complications of fluoroscopically guided interlaminar cervical epidural injections. Complications included increased neck pain (6.7%), non-positional headaches (4.6%), insomnia the night of injection (1.7%), vasovagal reactions (1.7%), facial flushing (1.5%), fever the night of the procedure (0.3%), and dural puncture (0.3%). The incidence of all complications was 16.8%. Derby et al (93) surveyed 17 International Spinal Intervention Society (ISIS) instructors who described a total of 5,978 cervical epidurals, of which 4,389 were interlaminar with 23 mild complications.

Waldman (94) reported a series of 790 cervical epidural steroid injections in 215 patients who were followed-up prospectively for 6 weeks after the procedure. Three patients had major complications and 3 had minor complications. The rate of complications per epidural steroid injection was 0.8%, whereas the incidence of major complications was 0.4%.

Infectious complications include cervical epidural abscess and meningitis (95-98). However, epidural steroid injection is an extremely rare cause of epidural abscess. Tang et al (99) evaluated predisposing factors leading to infection in an evaluation of 46 spinal epidural abscesses. Forty-six percent of patients had diabetes and 35% had a history of repeated and frequent intravenous injections of medications or illicit drugs, even though some patients with epidural ab-

Table 10. *Results of published studies of effectiveness of cervical interlaminar epidural steroid injections.*

Study	Study Characteristics	Methodological Quality Scoring	Participants	Pain Relief			Results	
				3 mos.	6 mos.	12 mos.	Short-term relief ≤ 6 months	Long-term relief > 6 months
Castagnera et al 1994 (74)	RA	55	Local anesthetic with steroids =14 Local anesthetic with steroids and morphine =10	79%	79%	79%	P	P
Stav et al 1993 (71)	RA	50	C = 17 T = 25	12% vs 68%	12% vs 68%	12% vs 68%	P	P
Pasqualucci et al 2007 (85)	RA	56	Single = 20 Continuous = 20 Over 180 days	NA	58% vs 74%	NA	P	NA

RA = randomized; C = control; T = treatment; vs = versus; P = positive; N = negative; NA = not available

scess formation had no identifiable risk factors (100). Huang et al (95) reported a case of cervical epidural abscess after epidural steroid injection resulting in decompressive laminectomy within the first 24 hours. The culture showed staphylococcus aureus, and the patient became quadriparetic with only partial recovery after 6 months. Waldman (96), in a letter to the editor, reported a single case of cervical epidural abscess after epidural steroid injection. The patient became symptomatic 72 hours after the third treatment with cervical epidural steroid injection which was followed by a decompressive laminectomy. The first surgery was unable to detect the abscess; however, a second surgery found the abscess and the culture showed staphylococcus aureus. Kricun et al (97) reported MRI findings in 5 cases of cervical epidural abscess. Papadakis et al (98) reported cervical paravertebral abscess following injection of corticosteroids. Cervical epidural abscess also has been reported following a trigger point injection (101).

Intravascular penetration, bleeding, and hematoma formation is a complication of cervical epidural injections, though rare. Intravascular penetration may occur even with negative aspiration (102). It is expected that intravascular penetration is a fairly common phenomenon with cervical interlaminar epidurals (103). However, clinically significant epidural hematoma are extremely rare (104,105). Williams et al (103) in 1990 presented a case of epidural hematoma following steroid injection, the complication occurring on the seventh such injection over a 2-year period for chronic spinal pain. Surgical decompression was required to alleviate the symptoms of paralysis and anesthesia. Others have reported multiple cases (106,107). Stoll and Sanchez (106) reported a large cervical epidural hematoma in a healthy 34-year-old man with no evidence of coagulopathy and not taking antiplatelet medication developing 8 days after a cervical epidural steroid injection and resulting in acute cervical myelopathy. Following prompt surgical evaluation of the clot, the patient made a near complete recovery. LaBan et al (107) reported 2 cases of epidural hematomas along with a description of 4 other cases previously reported. The first patient, a 36-year-old female developed a hematoma after her second injection with symptoms of numbness and tingling in both hands with the hematoma extending from C3 to T3. Following emergent surgical evacuation of the hematoma, she recovered partially. The second case was a 79-year-old female receiving Coumadin which had been prescribed for atrial fibrillation. Coumadin was discontinued and she was started on IV heparin. She was given an epidural corticosteroid injection 2 days later and subsequently developed paraparesis with a diagnosis of hematoma from T2 to T8 with cord compression. Despite an emergency decompressive laminectomy, she remained paraparetic with both a neurogenic bowel and bladder.

Vascular complications include vasospasms and embolic phenomena (108), whereas neurologic complications include intrinsic spinal cord damage, nerve root injury or damage, paraplegia, increased radicular pain, onset of complex regional pain syndrome, seizures, and headaches. Further, while neurologic injuries are uncommon, they can result from epidural abscess or epidural hematoma. Subdural hematoma, intracranial air, etc., have been reported. Subdural or subarachnoid injection will result in extensive spread of local anesthetic and serious consequences. Respiratory events are extremely rare but can lead to pneumothorax, recurrent laryngeal nerve injury, hoarseness of the voice, and dysphonia. A subdural hematoma after cervical epidural steroid injection with subsequent development of acute quadriplegia ultimately resulting in death has been reported (109). All of the following complications following cervical epidural injections have also been reported: multiple subdural hemorrhages (110); inadvertent subdural spread complicating injection of cervical epidural steroid with local anesthetic (111-113); intrinsic spinal cord damage and spinal cord infarction (114-116); neuropathic pain (117); pneumocephalus (118,119); subdural air (120); and epidural granuloma and intracranial hypotension (121).

Side effects related to the administration of steroids are generally attributed either to the chemistry or to the pharmacology of the steroids. The major theoretical 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 (122,123). Other complications include transient blindness (124), retinal necrosis (125), central serous chorioretinopathy (126,127), persistent hiccups (128), flushing (129), chemical meningitis (130), retinal hemorrhage (131), and ce-

rebral venous sinus thrombosis (132). 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 (121-141).

Finally, radiation exposure is also a potential problem with damage to eyes, skin, and gonads (142-144).

Discussion

This systematic review evaluated the effectiveness of cervical interlaminar epidural injections in patients with chronic neck and upper extremity pain and illustrated an indicated Level II-1 evidence for cervical interlaminar epidural injections with steroids for patients with chronic neck and upper extremity pain. The recommendation provided based on Guyatt et al's (70) criteria is with 1C/strong recommendation, which may change when higher quality evidence becomes available.

In contrast to caudal and lumbar epidural systematic reviews, studies of cervical epidural steroid injections have been rare, even though they have been included in some guidelines and systematic reviews (2,53). However, the limitations of this review include the paucity of literature and lack of randomized trials performed under fluoroscopy.

Cervical epidural steroid injections have been studied since 1985 (73). Historically, cervical epidural steroid injections originated from Pagés description of needle placement into the lumbar epidural space based on obstruction of free flow of spinal fluid from the needle and lack of resistance to injection of local anesthetic in 1921 (145). Dogliotti (146) was the first to describe the technique of cervical epidural block and also the first to describe, in 1933, the loss of resistance technique. The underlying mechanism of action of epidurally administered steroid and local anesthetic injection is still not well understood. A common problem encountered with any epidural injection is inaccurate needle placement, leading to inaccurate placement of the injectate (2,48,53). Consequently, proponents for fluoroscopic guidance in epidural steroid injections advocate utilizing this technique in order to assure that medications reach the appropriate and desired intervertebral space (48). In a study of 38 interlaminar cervical epidural steroid injections, they found a 53% rate of false loss of resistance during the first attempt to enter the epidural space. They suggested using fluoroscopy can improve the accuracy of needle placement and medication delivery. Even with second and third attempts, the success rate improved only to 75% with loss of resistance technique without fluoroscopy (147). In addition, it was also shown that when cervical epidural steroid injections are performed in the midline at C6/7 and C7/T1 under fluoroscopy, the contrast consistently covers the dorsal cervical epidural space bilaterally, irrespective of the volume used or neck flexion angle used (148). Further, fluoroscopic guidance also helps to avoid potential intravascular injections (149). Fluoroscopic utilization with contrast injection will also delineate multiple filling patterns including subdural and subarachnoid patterns. Even though the underlying mechanism of action of epidurally administered steroid and local anesthetic is not well understood, it is believed that the achieved neural blockade alters or interrupts nociceptive input, reflex mechanism of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities (2,48,53,121,122). Further, corticosteroids have been shown to reduce inflammation by inhibiting either the synthesis or release of a number of pro-inflammatory mediators and by causing a reversible local anesthetic effect (85,121,122,150-157). The emerging evidence also shows that the long-lasting effect may be obtained with local anesthetics with or without steroids (158-177). Further, it has been shown in rat experiments that nerve root infiltration prevented mechanical allodynia, even though no additional benefit from using corticosteroid was identified (157). Thus, it is suggested that corticosteroid may be unnecessary for nerve root blocks; in fact, this concept has been reinforced by numerous randomized and observational studies (169,171,174-186). Finally, in evaluation of epidural local anesthetic plus corticosteroid for the treatment of cervical brachial radicular pain with either a single injection or a continuous infusion (85), continuous epidural showed better control of chronic cervicobrachial pain compared with single injection, even though a corticosteroid was utilized in both injections. Thus, local anesthetic provides an independent effect or an additive effect.

Conclusion

The results of this systematic evaluation of cervical interlaminar epidural injections showed that they have a significant effect in relieving chronic intractable pain of cervical origin and also provide

long-term relief with indicated evidence of Level II-1 with a 1C/strong recommendation. However, evidence must be looked at on a regular basis and the data needs to be updated if further evidence becomes available.

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References

1. Hogg-Johnson S, van der Velde G, Carroll LJ, Holm LW, Cassidy JD, Guzman J, Côté P, Haldeman S, Ammendolia C, Carragee E, Hurwitz E, Nordin M, Peloso P, Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. The burden and determinants of neck pain in the general population: Results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine* 2008; 33:S39-S51.
2. Boswell MV, Trescot AM, Datta S, Schultz DM, Hansen HC, Abdi S, Sehgal N, Shah RV, Singh V, Benyamin RM, Patel VB, Buenaventura RM, Colson JD, Cordner HJ, Epter RS, Jasper JF, Dunbar EE, Atluri SL, Bowman RC, Deer TR, Swicegood JR, Staats PS, Smith HS, Burton AW, Kloth DS, Giordano J, Manchikanti L. Interventional techniques: Evidence-based practice guidelines in the management of chronic spinal pain. *Pain Physician* 2007; 10:7-111.
3. Côté P, Cassidy JD, Carroll L. The Saskatchewan Health and Back Pain Survey. The prevalence of neck pain and related disability in Saskatchewan adults. *Spine* 1998; 23:1689-1698.
4. Peloso PMJ, Gross A, Haines T, Trinh K, Goldsmith CH, Burnie SJ, Cervical Overview Group. Medicinal and injection therapies for mechanical neck disorders. *Cochrane Database Syst Rev* 2007; 3:CD000319.
5. Linton SJ, Hellsing AL, Hallden K. A population based study of spinal pain among 35–45-year old individuals. *Spine* 1998; 23:1457-1463.
6. Bot SD, van der Waal JM, Terwee CB, van der Windt DA, Schellevis FG, Bouter LM, Dekker J. Incidence and prevalence of complaints of the neck and upper extremity in general practice. *Ann Rheum Dis* 2005; 64:118-123.
7. Croft PR, Lewis M, Papageorgiou AC, Thomas E, Jayson MI, Macfarlane GJ, Silman AJ. Risk factors for neck pain: A longitudinal study in the general population. *Pain* 2001; 93:317-325.
8. Côté P, Cassidy JD, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: A population-based cohort study. *Pain* 2004; 112:267-273.
9. Enthoven P, Skargren E, Oberg B. Clinical course in patients seeking primary care for back or neck pain: A prospective 5-year follow-up of outcome and health care consumption with subgroup analysis. *Spine* 2004; 29:2458-2465.
10. Côté P, Kristman V, Vidmar M, Van Eerd D, Hogg-Johnson S, Beaton D, Smith PM. The prevalence and incidence of work absenteeism involving neck pain: A cohort of Ontario lost-time claimants. *Spine* 2008; 33:S192-S198.
11. Côté P, van der Velde G, Cassidy JD, Carroll LJ, Hogg-Johnson S, Holm LW, Carragee EJ, Haldeman S, Nordin M, Hurwitz EL, Guzman J, Peloso PM, Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. The burden and determinants of neck pain in workers. Results of the Bone and Joint Decade 2000–2010 Task Force on Neck Pain and Its Associated Disorders. *Spine* 2008; 33:S60-S74.
12. Palmer KT, Walker-Bone K, Griffin MJ, Syddall H, Pannett B, Coggon D, Cooper C. Prevalence and occupational associations of neck pain in the British population. *Scand J Work Environ Health* 2001; 27:49-56.
13. Leroux I, Dionne CE, Bourbonnais R, Brisson C. Prevalence of musculoskeletal pain and associated factors in the Quebec working population. *Int Arch Occup Environ Health* 2005; 78:379-86.
14. Saskatchewan Workers' Compensation Board. Statistical Supplement 2005. www.wcbsask.com/WCBPortal/ShowProperty/WCBRepository/formsPublications/publications/annualPubs/2005StatisticalSummary//pdfContent. Accessed date: October 15, 2008.
15. Brattberg G, Thorslund M, Wikman A. The prevalence of pain in a general population. The results of a postal survey in a county of Sweden. *Pain* 1989; 37:215-222.
16. Spitzer WO, Leblanc FE, Dupuis M. Scientific approach to the assessment and management of activity related spinal disorders. *Spine* 1987; 7:S1-59.
17. Cassidy JD, Carroll LJ, Côté P, Lemstra M, Berglund A, Nygren A. Effect of eliminating compensation for pain and suffering on the outcome of insurance claims for whiplash injury. *N Engl J Med* 2000; 342:1179-1186.
18. Radanov BP, Sturzenegger M, De Stefano G, Schnidrig A. Relationship between early somatic, radiological, cognitive and psychosocial findings and outcome during a one-year follow-up in 117 patients suffering from common whiplash. *Br J Rheumatol* 1994; 33:442-448.
19. Bogduk N. Low back pain. *Clinical Anatomy of Lumbar Spine and Sacrum*, 4th edition. Churchill Livingstone, New York, 2005, pp 183-216.
20. Lotz JC, Ulrich JA. Innervation, inflammation, and hypermobility may characterize pathologic disc degeneration: Review of animal model data. *J Bone Joint Surg Am* 2006; 88:76-82.
21. Yin W, Bogduk N. The nature of neck pain in a private pain clinic in the United States. *Pain Med* 2008; 9:196-203.
22. Bogduk N, Aprill C. On the nature of neck pain, discography and cervical

zygapophysial joint blocks. *Pain* 1993; 54:213-217.

23. Lord SM, Barnsley L, Wallis BJ, Bogduk N. Chronic cervical zygapophysial joint pain with whiplash: A placebo-controlled prevalence study. *Spine* 1996; 21:1737-1745.
24. Manchukonda R, Manchikanti KN, Cash KA, Pampati V, Manchikanti L. Facet joint pain in chronic spinal pain: An evaluation of prevalence and false-positive rate of diagnostic blocks. *J Spinal Disord Tech* 2007; 20:539-545.
25. Manchikanti L, Boswell MV, Singh V, Pampati V, Damron KS, Beyer CD. Prevalence of facet joint pain in chronic spinal pain of cervical, thoracic, and lumbar regions. *BMC Musculoskelet Disord* 2004; 5:15.
26. Manchikanti L, Manchikanti K, Cash KA, Singh V, Giordano J. Age-related prevalence of facet joint involvement in chronic neck and low back pain. *Pain Physician* 2008; 11:67-75.
27. Manchikanti L, Singh V, Pampati V, Damron KS, Beyer CD, Barnhill RC. Is there correlation of facet joint pain in lumbar and cervical spine? An evaluation of prevalence in combined chronic low back and neck pain. *Pain Physician* 2002; 5:365-371.
28. Manchikanti L, Manchikanti KN, Pampati V, Brandon DE, Giordano J. The prevalence of facet-joint-related chronic neck pain in postsurgical and nonpostsurgical patients: A comparative evaluation. *Pain Pract* 2008; 8:5-10.
29. Barnsley L, Lord SM, Wallis BJ, Bogduk N. The prevalence of chronic cervical zygapophyseal joint pain after whiplash. *Spine* 1995; 20:20-26.
30. Manchikanti L, Singh V, Rivera J, Pampati V. Prevalence of cervical facet joint pain in chronic neck pain. *Pain Physician* 2002; 5:243-249.
31. Bogduk N. Pathology. In *Medical Management of Acute Cervical Radicular Pain*. Newcastle Bone and Joint Institute, Newcastle, 1999, pp 13-18.
32. McCarron RF, Wimpee MW, Hudkins PG, Laros GS. The inflammatory effects of nucleus pulposus: A possible element in the pathogenesis of low back pain. *Spine* 1987; 12:760-764.
33. Olmarker K, Blomquist J, Stromberg J, Nannmark U, Thomsen P, Rydevik B. Inflammatogenic properties of nucleus pulposus. *Spine* 1995; 20:665-669.
34. Olmarker K, Nordborg C, Larsson K, Rydevik B. Ultrastructural changes in spinal nerve roots induced by autologous nucleus pulposus. *Spine* 1996; 27:411-414.
35. Kawakami M, Tamaki T, Hashizume H, Weinstein JN, Meller ST. The role of phospholipase A2 and nitric oxide in pain-related behavior produced by an allograft of intervertebral disc material to the sciatic nerve of the rat. *Spine* 1997; 22:1074-1079.
36. Kang JD, Georgescu HI, McIntyre-Larkin L, Stefanovic-Racic M, Evans CH. Herniated cervical intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E2. *Spine* 1995; 20: 2373-2378.
37. Kelsey JL, Githens PB, Walter SD, Southwick WO, Weil U, Holford TR, Ostfeld AM, Calogero JA, O'Connor T, White AA 3rd. An epidemiologic study of acute prolapsed cervical intervertebral disc. *J Bone Joint Surg Am* 1984; 66:907-914.
38. Kondo K, Molgaard CA, Kurland LT, Onofrio BM. Protruded intervertebral cervical disk: Incidence and affected cervical level in Rochester, Minnesota, 1950 through 1974. *Minn Med* 1981; 64:751-753.
39. Brain WR, Northfield D, Wilkinson M. The neurological manifestations of cervical spondylosis. *Brain* 1952; 75:187-225.
40. Arnold JG. The clinical manifestation of spondylochondrosis (spondylosis) of the cervical spine. *Ann Surg* 1955; 141:872-889.
41. Bohlman HH, Emery SE. The pathophysiology of cervical spondylosis and myelopathy. *Spine* 1988; 13:843-846.
42. Holt S, Yates PO. Cervical spondylosis and nerve root lesions: Incidence at routine necropsy. *J Bone Joint Surg Br* 1966; 48:407.
43. Kang JD, Bohlman HH. Current concepts review: Evaluation and treatment of cervical spondylotic myelography. *Pittsburgh Ortho J* 1994; 5:14-25.
44. Yabuki S, Kikuchi S, Olmarker K, Myers RR. Acute effects of nucleus pulposus on blood flow and endoneurial fluid pressure in rat dorsal root ganglia. *Spine* 1998; 23:2517-2523.
45. Genevay S, Finckh A, Payer M, Mezin F, Tessitore E, Gabay C, Guerne PA. Elevated levels of tumor necrosis factor-alpha in periradicular fat tissue in patients with radiculopathy from herniated disc. *Spine* 2008; 33:2041-2046.
46. Sugiura A, Ohtori S, Yamashita M, Inoue G, Yamauchi K, Koshi T, Suzuki M, Norimoto M, Orita S, Eguchi Y, Takahashi Y, Watanabe TS, Ochiai N, Takaso M, Takahashi K. Existence of nerve growth factor receptors, tyrosine kinase a and p75 neurotrophin receptors in intervertebral discs and on dorsal root ganglion neurons innervating intervertebral discs in rats. *Spine* 2008; 33:2047-2051.
47. Yamashita M, Ohtori S, Koshi T, Inoue G, Yamauchi K, Suzuki M, Takahashi K. Tumor necrosis factor-alpha in the nucleus pulposus mediates radicular pain, but not increase of inflammatory peptide, associated with nerve damage in mice. *Spine* 2008; 33:1836-1842.
48. Botwin KP, Guirguis R. Cervical interlaminar epidural steroid injections. In Manchikanti L, Singh V (eds). *Interventional Techniques in Chronic Spinal Pain.* ASIPP Publishing, Paducah, KY 2007; pp 401-422.
49. Specialty Utilization data files from CMS: www.cms.hhs.gov/physicians/pfs/
50. Manchikanti L. Medicare in interventional pain management: A critical analysis. *Pain Physician* 2008; 11:13-42.
51. Manchikanti L. Health Care Reform in the United States: Radical Surgery Needed Now More Than Ever. *Pain Physician* 2007; 10:607-626.
52. Manchikanti L, Boswell MV. Interventional techniques in ambulatory surgical centers: A look at the new payment system. *Pain Physician* 2007; 10:627-650.
53. Abdi S, Datta S, Trescot AM, Schultz DM, Adlaka R, Atluri SL, Smith HS, Manchikanti L. Epidural steroids in the management of chronic spinal pain: A systematic review. *Pain Physician* 2007; 10:185-212.
54. Manchikanti L, Singh V, Derby R, Schultz DM, Benyamin RM, Prager JP, Hirsch JA. Reassessment of evidence synthesis of occupational medicine practice guidelines for interventional pain management. *Pain Physician* 2008; 11:393-482.
55. Koes BW, Scholten RJ, Mens JMA, Bouter LM. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. *Pain* 1995; 63:279-288.

56. West S, King V, Carey TS, Lohr KN, McKoy N, Sutton SF, Lux L. *Systems to Rate the Strength of Scientific Evidence*, Evidence Report, Technology Assessment No. 47. AHRQ Publication No. 02-E016. Rockville, MD: Agency for Healthcare Research and Quality, 2002. www.thecre.com/pdf/ahrq-system-strength.pdf
57. Atluri S, Datta S, Falco FJ, Lee M. Systematic review of diagnostic utility and therapeutic effectiveness of thoracic facet joint interventions. *Pain Physician* 2008; 11:611-629.
58. Conn A., Buenaventura RM, Datta S, Abdi S, Diwan S. Systematic review of caudal epidural injections in the management of chronic low back pain. *Pain Physician* 2009; 12:109-135.
59. Parr AT, Diwan S, Abdi S. Lumbar interlaminar epidural injections in managing chronic low back and lower extremity pain: A systematic review. *Pain Physician* 2009; 12:163-188.
60. Helm S, Hayek S, Benyamin R, Manchikanti L. Systematic review of the effectiveness of thermal annular procedures in treating discogenic low back pain. *Pain Physician* 2009; 12:207-232.
61. van Tulder M, Furlan A, Bombardier C, Bouter L, Editorial Board of the Cochrane Collaboration Back Review Group. Updated method guidelines for systematic reviews in the Cochrane Collaboration Back Review Group. *Spine* 2003; 28:1290-1299.
62. Staal JB, de Bie R, de Vet HC, Hildebrandt J, Nelemans P. Injection therapy for subacute and chronic low-back pain. *Cochrane Database Syst Rev* 2008; 3:CD001824.
63. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain* 2004; 8:283-291.
64. Bombardier C. Outcome assessments in the evaluation of treatment of spinal disorders: Summary and general recommendations. *Spine* 2000; 25:3100-3103.
65. Manchikanti L. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part 1: Introduction and general considerations. *Pain Physician* 2008; 11:161-186.
66. Manchikanti L, Hirsch JA, Smith HS. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part 2: Randomized controlled trials. *Pain Physician* 2008; -11:717-773.
67. Manchikanti L, Smith HS, Hirsch JA. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part 3: Systematic reviews and meta-analyses of randomized trials. *Pain Physician* 2009;12:35-72.
68. Manchikanti L, Smith HS, Hirsch JA. Evidence-based medicine, systematic reviews, and guidelines in interventional pain management: Part 4: Observational studies. *Pain Physician* 2009; 12:73-108.
69. Berg AO, Allan JD. Introducing the third U.S. Preventive Services Task Force. *Am J Prev Med* 2001; 20:21-35.
70. Guyatt G, Gutterman D, Baumann MH, Addrizzo-Harris D, Hylek EM, Phillips B, Raskob G, Lewis SZ, Schünemann H. Grading strength of recommendations and quality of evidence in clinical guidelines. Report from an American College of Chest Physicians Task Force. *Chest* 2006; 129:174-181.
71. Stav A, Ovadia L, Sternberg A, Kaadan M, Weksler N. Cervical epidural steroid injection for cervicobrachialgia. *Acta Anaesthesiol Scand* 1993; 37:562-566.
72. Bush K, Hillier S. Outcome of cervical radiculopathy treated with periradicular/epidural corticosteroid injections: A prospective study with independent clinical review. *Eur Spine J* 1996; 5:319-325.
73. Pawl RP, Anderson W, Shulman M. Effect of epidural steroids in the cervical and lumbar region on surgical intervention for discogenic spondylosis. *Clin J Pain* 1985; 1:181-185.
74. Castagnera L, Maurette P, Pointillart V, Vital JM, Erny P, Senegas J. Long term results of cervical epidural steroid injection with and without morphine in chronic cervical radicular pain. *Pain* 1994; 58:239-243.
75. Shulman J. Treatment of neck pain with cervical epidural steroid injection. *Reg Anesth* 1986; 11:92-94.
76. Rowlingson JC, Kirschenbaum LP. Epidural analgesic techniques in the management of cervical pain. *Anesth Analg* 1986; 65:938-942.
77. Purkis IE. Cervical epidural steroids. *Pain Clinic* 1986; 1:3-7.
78. Warfield CA, Biber MP, Crews DA, Dwarakanath GK. Epidural steroid injection as a treatment for cervical radiculitis. *Clin J Pain* 1988; 4:201-204.
79. Cicala RS, Thoni K, Angel JJ. Long-term results of cervical epidural steroid injections. *Clin J Pain* 1989; 5:143-145.
80. Proano FA, Morgan PJ, Hymes JA, Rosenblatt RM, Weiss JA. Cervical steroid epidural block for treatment of cervical herniated intervertebral discs. *Pain* 1990; 5:S87.
81. Manger D, Thomas PS. Epidural steroid injections in the treatment of cervical and lumbar pain syndromes. *Reg Anesth* 1991; 16:246.
82. Ferrante FM, Wilson SP, Iacobo C, Orav EJ, Rocco AG, Lipson S. Clinical classification as a predictor of therapeutic outcome after cervical epidural steroid injection. *Spine* 1993; 18:730-736.
83. Klein RG, Vaccaro AR, Cwik J, Seitchik S, Viscusi ER, Albert TJ. Efficacy of cervical epidural steroids in the treatment of cervical spine disorders. *Am J Anesthesiol* 2000; 9:547-552.
84. Catchlove RF, Braha R. The use of cervical epidural nerve blocks in the management of chronic head and neck pain. *Can Anaesth Soc J* 1984; 31:188-191.
85. Pasqualucci A, Varrassi G, Braschi A, Peduto VA, Brunelli A, Marinangeli F, Gori F, Colò F, Paladini A, Mojoli F. Epidural local anesthetic plus corticosteroid for the treatment of cervical brachial radicular pain: Single injection versus continuous infusion. *Clin J Pain* 2007; 23:551-557.
86. Kwon JW, Lee JW, Kim SH, Choi JY, Yeom JS, Kim HJ, Kwack KS, Moon SG, Jun WS, Kang HS. Cervical interlaminar epidural steroid injection for neck pain and cervical radiculopathy: Effect and prognostic factors. *Skeletal Radiol* 2007; 36:431-436.
87. Martelletti P, Di Sabato F, Granata M, Alampi D, Apponi F, Borgonuovo P, Reale C, Giacovazzo M. Epidural corticosteroid blockade in cervicogenic headache. *Eur Rev Med Pharmacol Sci* 1998; 2:31-36.
88. Martelletti P, Di Sabato F, Granata M, Alampi D, Apponi F, Borgonuovo P, Reale C, Giacovazzo M. Epidural steroid-based technique for cervicogenic headache diagnosis. *Funct Neurol* 1998; 13:84-87.

89. Grenier B, Castagnera L, Maurette P, Erny P, Senegas J. Chronic cervico-brachial neuralgia treated by cervical epidural injection of corticosteroids. Long-term results. *Ann Fr Anesth Reanim* 1995; 14:484-488.
90. Mori K, Yamashita J, Yamasaki S, Fukumit T. Management of cervical syndromes with epidural injection of steroid hormones. *Geka Chiryo* 1969; 21:397-404.
91. Botwin KP, Castellanos R, Raos, Hanna AF, Torres-Ramos FM, Gruber RD, Bouchlas CG, Fuoco GS. Complications of fluoroscopically guided interlaminar cervical injections. *Arch Phys Med Rehabil* 2003; 84:627-633.
92. Cicala RS, Westbrook L, Angel JJ. Side effects and complications of cervical epidural steroid injections. *J Pain Symptom Manage* 1989; 4:64-66.
93. Derby R, Lee SH, Kim BJ, Chen Y, and Seo KS. Complications following cervical epidural steroid injections by expert interventionalists in 2003. *Pain Physician* 2004; 7:445-449.
94. Waldman SD. Complications of cervical epidural nerve block with steroids: A prospective study of 790 consecutive blocks. *Reg Anaesth* 1989; 14:149-151.
95. Huang RC, Shapiro GS, Lim M, Sandhu HS, Lutz GE, Herzog RJ. Cervical epidural abscess after epidural steroid injection. *Spine* 2004; 29:E7-E9.
96. Waldman SD. Cervical epidural abscess after cervical epidural nerve block with steroids. *Anesth Analg* 1991; 72:717-718.
97. Kricun R, Shoemaker EI, Chovanes GI, Stephens HW. Epidural abscess of the cervical spine: MR findings in five cases. *AJR Am J Roentgenol* 1992; 158:1145-1149.
98. Papadakis CE, Chimona TS, Skoulakis CE, Prokopakis EP, Kyrmizakis DE, Velegrakis GA. Cervical prevertebral abscess owing to injection of corticosteroids. *J Otolaryngol* 2005; 34:254-257.
99. Tang H, Lin H, Liu Y, Li CM. Spinal epidural abscess-experience with 46 patients and evaluation of prognostic factors. *J Infect* 2002; 45:76-81.
100. Anand S, Maini L, Agarwal A, Sing T, Dhal AK, Dhaon BK. Spinal epidural abscess – a report of six cases. *Int Orthop* 1999; 23:175-177.
101. Elias M. Cervical epidural abscess following trigger point injection. *J Pain Symptom Manage* 1991; 9:71-72.
102. Ho KY. Vascular uptake of contract despite negative aspiration in interlaminar cervical epidural injection. *Pain Physician* 2006; 9:267-268.
103. Williams KN, Jackowski A, Evans PJ. Epidural haematoma requiring surgical decompression following repeated cervical epidural steroid injections for chronic pain. *Pain* 1990; 42:197-199.
104. Markham JW, Lynge HN, Stahlman GE. The syndrome of spontaneous spinal epidural hematoma. Report of three cases. *J Neurosurg* 1967; 26:334-341.
105. Yagi S, Hida K, Iwasaki Y, Abe H, Akino M, Saito H. Cervical epidural hematoma caused by cervical twisting after epidural anesthesia: A case report. *No Shinkei Geka* 1998; 26:235-242.
106. Stoll A, Sanchez M. Epidural hematoma after epidural block: Implications for its use in pain management. *Surg Neurol* 2002; 57:235-240.
107. LaBan MM, Kasturi G, Wang IM. Epidural corticosteroid injections precipitating epidural hematomas with spinal paresis. *Am J Phys Med Rehabil* 2007; 86:166-167.
108. MacLean CA, Bachman DT. Documented arterial gas embolism after spinal epidural injection. *Ann Emerg Med* 2001; 38:592-595.
109. Reitman CA, Watters W 3rd. Subdural hematoma after cervical steroid injection. *Spine* 2002; 27:E174-E176.
110. Mendelson J, Muppidi S, Silberstein S. Multiple intracerebral hemorrhages after cervical epidural injections. *Neurology* 2008; 70:2415-2416.
111. Oberoi G. Inadvertent subdural spread complicating injection of cervical epidural steroid with local anaesthetic. *Anaesth Intensive Care* 2004; 32:846.
112. Russo MA. Inadvertent subdural spread complicating cervical epidural steroid injection. *Anaesth Intensive Care* 2004; 32:145-146.
113. Bansal S, Turtle MJ. Inadvertent subdural spread complicating cervical epidural steroid injection with local anaesthetic agent. *Anaesth Intensive Care* 2003; 31:570-572.
114. Hodges SD, Castleberg RL, Miller T, Ward R, Thornburg C. Cervical epidural steroid injection with intrinsic spinal cord damage. Two case reports. *Spine* 1998; 23:2137-2142.
115. Arpa J, Lara M, Cruz Martinez A, Perez Jimenez A. Cervical spinal cord infarction caused by the use of epidural morphine. *Neurologia* 1992; 7:240-241.
116. Tanaka A, Nakazawa S, Nishikawa K, Saito S. Spinal cord infarction following multiple epidural injections. *Pain Clinic* 2004; 16:207-211.
117. Field J, Rathmell JP, Stephenson JH, Katz NP. Neuropathic pain following cervical epidural steroid injection. *Anesthesiology* 2000; 93:885-888.
118. Simopoulos T, Peeters-Asdourian C. Pneumocephalus after cervical epidural steroid injection. *Anesth Analg* 2001; 92:1576-1577.
119. Hawley JS, Ney JP, Swanberg MM. Subarachnoid pneumocephalus from epidural steroid injection. *Headache* 2005; 45:247-248.
120. Katz JA, Lukin R, Bridenbaugh PO, Gunzenhauser L. Subdural intracranial air: An unusual cause of headache after epidural steroid injection. *Anesthesiology* 1991; 74:615-618.
121. Dietrich CL, Smith CE. Epidural granuloma and intracranial hypotension resulting from cervical epidural steroid injection. *Anesthesiology* 2004; 100:445-447.
122. Manchikanti L. Role of neuraxial steroids in interventional pain management. *Pain Physician* 2002; 5:182-199.
123. Manchikanti L. Pharmacology of neuraxial steroids. In Manchikanti L, Singh V (eds). *Interventional Techniques in Chronic Spinal Pain.* ASIPP Publishing, Paducah KY, 2007; pp 167-184.
124. Young WF. Transient blindness after lumbar epidural steroid injection: A case report and literature review. *Spine* 2002; 27:E476-E477.
125. Browning DJ. Acute retinal necrosis following epidural steroid injections. *Am J Ophthalmol 2003;* 136:192-194.
126. Iida T, Spaide RF, Negrao SG, Carvalho CA, Yannuzzi LA. Central serous chorioretinopathy after epidural corticosteroid injection. *Am J Ophthalmol* 2001; 132:423-425.
127. Pizzimenti JJ, Daniel KP. Central serous chorioretinopathy after epidural steroids. *Pharmacotherapy* 2005; 25:1141-1146.
128. McAllister RK, McDavid AJ, Meyer TA, Bittenbinder TM. Recurrent persistent hiccups after epidural steroid injection and analgesia with bupivacaine. *Anesth Analg* 2005; 100:1834-1836.
129. Everett CR, Baskin MN, Novoseletsky

D, Speach D, Patel R. Flushing as a side effect following lumbar transforaminal epidural steroid injection. *Pain Physician* 2004; 7:427-429.

130. Gutknecht DR. Chemical meningitis following epidural injections of corticosteroids (Letter). *Am J Med* 1987; 82:570.
131. Kusher FH, Olson JC. Retinal hemorrhage as a consequence of epidural steroid injection. *Arch Opthalmol* 1995; 113:309-313.
132. Milhaud D, Heroum C, Charif M, Saulnier P, Pages M, Blard JM. Dural puncture and corticotherapy as risk factors for cerebral venous sinus thrombosis. *Eur J Neruol* 2000; 7:123-124.
133. Manchikanti L, Pampati V, Beyer CD, Damron KS, Cash KA, Moss TL. The effect of neuraxial steroids on weight and bone mass density: A prospective evaluation. *Pain Physician* 2000; 3:357-366.
134. Kingery WS, Castellote JM, Maze M. Methylprednisolone prevents the development of autotomy and neuropathic edema in rats, but has no effect on nociceptive thresholds. *Pain* 1999; 80:555-566.
135. Delaney TJ, Rowlingson JC, Carron H, Butler A. Epidural steroid effects on nerves and meninges. *Anesth Analg* 1980; 58:610-614.
136. Mackinnon SE, Hudson AR, Gentili F, Kline DG, Hunter D. Peripheral nerve injection injury with steroid agents. *Plast Reconstr Surg* 1982; 69:482-489.
137. Chino N, Awad EA, Kottke FJ. Pathology of propylene glycol administered by perineural and intramuscular injection in rats. *Arch Phys Med Rehab* 1974; 55:33-38.
138. Abram SE, Marsala M, Yaksh TL. Analgesic and neurotoxic effects of intrathecal corticosteroids in rats. *Anesthesiology* 1994; 81:1198-1205.
139. Benzon HT. Epidural steroid injections for low back pain and lumbosacral radiculopathy. *Pain* 1986; 24:277-295.
140. Latham JM, Fraser RD, Moore RJ, Blumbergs PC, Bogduk N. The pathologic effects of intrathecal betamethasone. *Spine* 1997; 22:1558-1562.
141. Robustelli della Cuna FS, Mella M, Magistrali G, Ricci M, Losurdo A, Goglio AM. Stability and compatibility of methylprednisolone acetate and ropivacaine hydrochloride in polypropylene syringes for epidural administration. *Am J Health Syst Pharm* 2001; 58:1753-1756.
142. Manchikanti L, Cash KA, Moss TL, Pampati V. Effectiveness of protective measures in reducing risk of radiation exposure in interventional pain management: A prospective evaluation. *Pain Physician* 2003; 6:301-305.
143. Manchikanti L, Cash KA, Moss TL, Rivera JJ, Pampati V. Risk of whole body radiation exposure and protective measures in fluoroscopically guided interventional techniques: A prospective evaluation. *BMC Anesthesiol* 2003; 3:2.
144. Manchikanti L, Cash KA, Moss TL, Pampati V. Radiation exposure to the physician in interventional pain management. *Pain Physician* 2002; 5:385-393.
145. Pagés E. Anesthesia metamérica. *Rev Sanid Mil Madr* 1921; 11:351-385.
146. Dogliotti AM. Segmental peridural anesthesia. *Am J Surg* 1933; 20:107-118.
147. Stojanovic MP, Vu TN, Caneris O, Slezak J, Cohen SP, Sang CN. The role of fluoroscopy in cervical epidural steroid injections: An analysis of contrast dispersal patterns. *Spine* 2002; 27:509-514.
148. Goel A, Pollan JJ. Contrast flow characteristics in the cervical epidural space: An analysis of cervical epidurograms. *Spine* 2006; 31:1576-1579.
149. Furman MB, Giovanniello MT, O'Brien EM. Incidence of intravascular penetration in transforaminal cervical epidural steroid injections. *Spine* 2003; 28:21-25.
150. Byrod G, Otani K, Brisby H, Rydevik B, Olmarker K. Methylprednisolone reduces the early vascular permeability increase in spinal nerve roots induced by epidural nucleus pulposus application. *J Orthop Res* 2000; 18:983-987.
151. Flower RJ, Blackwell GJ. Anti-inflammatory steroid induced biosynthesis of a phospholipase A2 inhibitor which prevents prostaglandin generation. *Nature* 1979; 278:456-459.
152. Lundin A, Magnuson A, Axelsson K, Nilsson O, Samuelsson L. Corticosteroids preoperatively diminishes damage to the C-fibers in microscopic lumbar disc surgery. *Spine* 2005; 30:2362-2367.
153. Hua SY, Chen YZ. Membrane receptor-mediated electrophysiological effects of glucocorticoid on mammalian neurons. *Endocrinology* 1989; 124:687-691.
154. Hayashi N, Weinstein JN, Meller ST, Lee HM, Spratt KF, Gebhart GF. The effect of epidural injection of betamethasone or bupivacaine in a rat model of lumbar radiculopathy. *Spine* 1998; 23:877-885.
155. Lee HM, Weinstein JN, Meller ST, Hayashi N, Spratt KF, Gebhart GF. The role of steroids and their effects on phospholipase A2: An animal model of radiculopathy. *Spine* 1998; 23:1191-1196.
156. Minamide A, Tamaki T, Hashizume H, Yoshida M, Kawakami M, Hayashi N. Effects of steroids and lipopolysaccharide on spontaneous resorption of herniated intervertebral discs: An experimental study in the rabbit. *Spine*1998; 23:870-876.
157. Tachihara H, Sekiguchi M, Kikuchi S, Konno S. Do corticosteroids produce additional benefit in nerve root infiltration for lumbar disc herniation. *Spine* 2008; 33:743-747.
158. Katz WA, Rothenberg R. The nature of pain: Pathophysiology. *J Clin Rheumatol* 2005; 11(2 suppl):S11-15.
159. Mao J, Chen LL. Systemic lidocaine for neuropathic pain relief. *Pain* 2000; 87:7-17.
160. Pasqualucci A. Experimental and clinical studies about the preemptive analgesia with local anesthetics. Possible reasons of the failure. *Minerva Anestesiol* 1998; 64:445-457.
161. Ferrante FM, Paggioli J, Cherukuri S, Arthru GR. The analgesic response to intravenous lidocaine in the treatment of neuropathic pain. *Anesth Analg* 1996; 82:91-97.
162. Arner S, Lindblom U, Meyerson BA, Molander C. Prolonged relief of neuralgia after regional anesthetic block. A call for further experimental and systematic clinical studies. *Pain* 1990; 43:287-297.
163. Lavoie PA, Khazen T, Filion PR. Mechanisms of the inhibition of fast axonal transport by local anesthetics. *Neuropharmacology* 1989; 28:175-181.
164. Bisby MA. Inhibition of axonal transport in nerves chronically treated with local anesthetics. *Exp Neurol* 1975; 47:481-489.
165. Wertheim HM, Rovenstine EA. Suprascapular nerve block. *Anesthesiology* 1941; 2:541.
166. Riew KD, Park JB, Cho YS, Gilula L, Patel A, Lente LG, Bridwell KH. Nerve root blocks in the treatment of lumbar radicular pain. A minimum five-year fol-

low-up. *J Bone Joint Surg Am* 2006; 88:1722-1725.

167. Manchikanti L. Interventional pain management: Past, present, and future. The Prithvi Raj lecture: Presented at the 4th World Congress-World Institute of Pain, Budapest, 2007. *Pain Pract* 2007; 7:357-371.
168. Abram SE, Likavec MJ. Pain syndromes and rationale for management. Neurogenic pain. In Raj P (ed). *Practical Management of Pain*. Year Book Medical Publishers, Chicago, 1986, pp 182-191.
169. Manchikanti L, Singh V, Rivera JJ, Pampati V, Beyer CD, Damron KS, Barnhill RC. Effectiveness of caudal epidural injections in discogram positive and negative chronic low back pain. *Pain Physician* 2002; 5:18-29.
170. Bonica JJ. Current role of nerve blocks in diagnosis and therapy of pain. In Bonica JJ (ed). *Advances in Neurology*, Vol. 4. Raven Press, New York, 1974, pp 445-453.
171. Manchikanti L, Pampati V, Rivera JJ, Beyer CD, Damron KS, Barnhill RC. Caudal epidural injections with Sarapin steroids in chronic low back pain. *Pain Physician* 2001; 4:322-335.
172. Raj PP. Prognostic and therapeutic local anaesthetic blockade. In Cousins MJ, Bridenbaugh PO (eds). *Neural Blockade*. Lippincott, Philadelphia, 1988, pp 900-901.
173. Sato C, Sakai A, Ikeda Y, Suzuki H, Sakamoto A. The prolonged analgesic effect of epidural ropivacaine in a rat model of neuropathic pain. *Anesth Analg* 2008; 106:313-320.
174. Manchikanti L, Singh V, Falco FJ, Cash KA, Pampati V. Lumbar facet joint nerve blocks in managing chronic facet joint pain: One-year follow-up of a randomized, double-blind controlled trial: Clinical Trial NCT00355914. *Pain Physician* 2008; 11:121-132.
175. Manchikanti L, Singh V, Falco FJ, Cash KA, Fellows B. Cervical medial branch blocks for chronic cervical facet joint pain: A randomized double-blind, controlled trial with one-year follow-up. *Spine* 2008; 33:1813-1820.
176. Manchikanti L, Singh V, Falco FJE, Cash KA, Pampati V. Effectiveness of thoracic medial branch blocks in managing chronic pain: A preliminary report of a randomized, double-blind controlled trial: Clinical trial NCT00355706. *Pain Physician* 2008; 11:491-504.
177. Kawakami M, Weinstein JN, Chatani K, Spratt KF, Meller ST, Gebhart GF. Experimental lumbar radiculopathy. Behavioral and histologic changes in a model of radicular pain after spinal nerve root irritation with chromic gut ligatures in the rat. *Spine* 1994; 19:1795-1802.
178. Manchikanti L, Cash KA, McManus CD, Pampati V, Smith HS. Preliminary results of randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 1. Discogenic pain without disc herniation or radiculitis. *Pain Physician* 2008; 11:785-800.
179. Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. Preliminary results of randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 2. Disc herniation and radiculitis. *Pain Physician* 2008; 11:801-815.
180. Manchikanti L, Singh V, Cash KA, Pampati V, Datta S. Preliminary results of randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 3. Post surgery syndrome. *Pain Physician* 2008; 11:817-831.
181. Manchikanti L, Cash KA, McManus CD, Pampati V, Abdi S. Preliminary results of randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 4. Spinal stenosis. *Pain Physician* 2008; 11:833-848.
182. Manchikanti L. Transforaminal lumbar epidural steroid injections. *Pain Physician* 2000; 3:374-398.
183. Manchikanti KN, Pampati V, Damron KS, McManus CD. A double-blind, controlled evaluation of the value of Sarapin in neural blockade. *Pain Physician* 2004; 7:59-62.
184. Manchikanti L, Damron KS, Cash KA, Manchukonda R, Pampati V. Therapeutic medial branch blocks in managing chronic neck pain: A preliminary report of a randomized, double-blind, controlled trial: Clinical Trial NCT00033272. *Pain Physician* 2006; 9:333-346.
185. Manchikanti L, Manchikanti KN, Manchukonda R, Pampati V, Cash KA. Evaluation of therapeutic thoracic medial branch block effectiveness in chronic thoracic pain: A prospective outcome study with minimum 1-year follow up. *Pain Physician* 2006; 9:97-105.
186. Manchikanti L, Manchikanti K, Manchukonda R, Cash KA, Damron KS, Pampati V, McManus CD. Evaluation of lumbar facet joint nerve blocks in the management of chronic low back pain: A preliminary report of a randomized, double-blind controlled trial: Clinical Trial NCT000355914. *Pain Physician* 2007; 10:425-440.