

Randomized Trial

Effectiveness of Thoracic Medial Branch Blocks in Managing Chronic Pain: A Preliminary Report of a Randomized, Double-Blind Controlled Trial; Clinical Trial NCT00355706

Laxmaiah Manchikanti, MD¹, Vijay Singh, MD², Frank J.E. Falco, MD³, Kimberly A. Cash, RT¹, and Vidyasagar Pampati, MSc¹

From: ¹Pain Management Center of Paducah, Paducah, KY; ²Pain Diagnostics Associates, Niagara, WI, and ³Mid Atlantic Spine & Pain Specialists of Newark, DE

Dr. Manchikanti is Medical Director of the Pain Management Center of Paducah, Paducah, KY, and Associate Clinical Professor of Anesthesiology and Perioperative Medicine, University of Louisville, KY. Dr. Singh is Medical Director, Pain Diagnostics Associates, Niagara, WI

Dr. Falco is Clinical Assistant Professor, Temple University Medical School, Philadelphia, PA, and Medical Director of the Mid Atlantic Spine & Pain Specialists, Newark, DE.

Ms. Cash is a Research Coordinator at the Pain Management Center of Paducah, Paducah, KY

Mr. Pampati is a Statistician at the Pain Management Center of Paducah, Paducah, KY

Address correspondence: Laxmaiah Manchikanti, MD
2831 Lone Oak Road
Paducah, Kentucky 42003
E-mail: drlm@thepainmd.com

Disclaimer: There was no external funding in the preparation of this manuscript.

Conflict of interest: None.

Manuscript received: 05/28/2008
Accepted for publication: 06/30/2008

Free full manuscript:

Background: Thoracic facet joints have been implicated as the source of chronic pain in the mid back or upper back in 34% to 48% of the patients. Various therapeutic techniques utilized in managing chronic thoracic pain of facet joint origin include intraarticular injections, medial branch blocks, and radiofrequency neurotomy of thoracic facet joint nerves.

Objective: To determine the clinical effectiveness of therapeutic local anesthetic medial branch blocks with or without steroid in managing chronic function-limiting mid back or upper back pain of facet joint origin.

Design: A randomized, double-blind, controlled trial.

Setting: An interventional pain management private practice, a tertiary referral center, in the United States.

Methods: A total of 48 patients were included, with 24 patients in each of the local anesthetic and steroid groups. All of the patients met the diagnostic criteria of thoracic facet joint pain by means of comparative, controlled diagnostic blocks and the inclusion criteria. Group I patients received thoracic medial branch blocks with bupivacaine, whereas Group II patients received thoracic medial branch blocks with bupivacaine and non-particulate betamethasone.

Outcome Measures: Numeric pain scores (NRS), Oswestry Disability Index (ODI), opioid intake, and return to work status. All outcomes were assessed at baseline, 3 months, 6 months, and 12 months. Significant pain relief was defined as > 50% pain relief. Significant functional improvement was defined as 40% reduction of ODI.

Results: In Group I, 79% of patients showed significant pain relief and functional improvement at 3 months, 6 months, and 12 months, a significant change from baseline. In Group II, 83%, 81%, and 79% of patients showed significant pain relief and functional improvement at 3 months, 6 months, and 12 months, a significant change from baseline. The majority of the patients experienced significant pain relief of 46 to 50 weeks, requiring approximately 3 to 4 treatments with an average relief of 16 weeks per episode of treatment.

Conclusion: The majority of the patients in both groups experienced significant pain relief and improvement in functional status. Therapeutic thoracic medial branch blocks, with or without steroid, may provide a management option for chronic function-limiting mid back or upper back pain of facet joint origin.

Key words: Chronic spinal pain, thoracic pain, thoracic facet or zygapophysial joint pain, facet joint nerve or medial branch blocks, comparative controlled local anesthetic blocks, therapeutic thoracic medial branch blocks

Pain Physician 2008; 11:4:491-504

The proportion of patients suffering from chronic upper or mid back pain secondary to thoracic disorders is relatively small in interventional pain management settings, ranging from 3% to 22% (1-3). The role of thoracic facet joints as a cause of chronic upper or mid back pain has received very little attention with only a few publications discussing these joints as the source of pain (1-3). Linton et al (4) estimated the prevalence of thoracic pain in 15% of the general population in contrast to 56% reporting low back pain and 44% reporting neck pain. Involvement of thoracic facet joints as a cause of chronic mid back and upper back pain was described in 1987 (5). Thoracic facet joint pain patterns were described by Dreyfuss et al in 1994 (6) and Fukui et al in 1997 (7). Thoracic facet joints have been implicated as the source of chronic pain in 34%-48% of patients with chronic mid back and upper back pain based on responses to controlled diagnostic blocks of these joints (8-13), in accordance with the criteria established by the International Association for the Study of Pain (IASP) (14).

Bogduk (15) postulated that, for any structure to be deemed a cause of back pain the structure should 1) have a nerve supply, 2) be able of causing pain of that similar to that seen clinically, ideally demonstrated in normal volunteers, 3) be susceptible to diseases or injuries that are known to be painful, and 4) have been shown to be a source of pain in patients, using diagnostic techniques of known reliability and validity. Based on the postulates of Bogduk (15), thoracic facet joints have been shown to have abundant nerve supply (6,7,12,16-23). The thoracic facet joints have been shown to be capable of causing pain similar to that seen clinically, in normal volunteers with persistent thoracic pain and referred pain in the chest wall (6,7); thoracic facet joints can be affected by osteoarthritis, rheumatoid arthritis, spondylitis, degeneration, inflammation, and injury leading to pain upon joint motion and restriction of motion; and thoracic facet joints have been shown to be a source of pain in patients, using diagnostic techniques of known reliability and validity (1-13). Further, multiple therapeutic techniques have been described in managing chronic thoracic pain of facet joint origin including intraarticular injections, medial branch blocks, and radiofrequency neurotomy with variable evidence (24-28). However, a paucity of literature on the role of thoracic pain in general, diagnostic, and therapeutic interventions specifically managing facet joints continues to exist.

Systematic reviews (25,26) have provided a lack of evidence for thoracic intraarticular injections, moderate evidence for thoracic medial branch blocks (27), and limited evidence for radiofrequency neurotomy of facet joint nerves (3,28). Consequently, thus far, the only effective modality in managing chronic thoracic pain of facet joint origin appears to involve therapeutic thoracic medial branch blocks (27). In addition, medial branch blocks have been described as an alternative to percutaneous radiofrequency neurotomy in cervical and lumbar spine in controlled trials (29-32). Radiofrequency neurotomy provides temporary or long-term relief of pain by denaturing the nerves that innervate the painful joint (33,34). In contrast, with thoracic medial branch blocks, the exact mechanism of therapeutic effect is not known. However, medial branch blocks may be repeated to reinstate the relief similar to radiofrequency neurotomy. Significant effectiveness of cervical and lumbar facet nerve blocks with or without steroids has been demonstrated in randomized, double-blind, controlled trials (29-32).

The literature for management of facet joint pain in the cervical and lumbar spine is abundant (11,24-26,29-34). While the prevalence of thoracic pain in general and facet joint pain in particular is less than lumbar and cervical spinal pain, thoracic spinal pain can be as chronic and disabling as neck and low back pain. Due to the lack of available evidence, thoracic facet joint interventions are considered as experimental or investigational.

In this study, we sought to evaluate the effectiveness of thoracic medial branch blocks in providing relief of chronic, function-limiting mid back and upper back pain in a randomized, double-blind, controlled evaluation. This is a preliminary report of one-year follow-up of 48 patients from scheduled 2-year follow-up.

METHODS

This evaluation was conducted in the United States on patients suffering with chronic, function-limiting, thoracic facet joint pain. The study site is an interventional pain management practice, a specialty referral center, in a private practice setting. The study was designed to meet clinical protocol criteria and CONSORT guidelines (35).

The study protocol was approved by the Institutional Review Board of the Ambulatory Surgery Center. The study was registered on the U.S. Clinical Trial Registry with an assigned number of NCT00355706.

Participants

Eligible patients with a confirmed diagnosis of thoracic facet joint pain by controlled comparative local anesthetic blocks were assigned to one of 2 groups with Group I constituting a nonsteroid group, and Group II encompassing a steroid group. Group I patients received medial branch blocks with injections of bupivacaine 0.25%, whereas Group II patients received medial branch blocks with a mixture of bupivacaine and non-particulate betamethasone. Non-particulate betamethasone (0.15 mg) was added to each mL of bupivacaine solution

Inclusion Criteria

Only patients with non-specific mid back or upper back pain were included. Patients suspected of disc related pain with radicular symptoms were excluded based on radiologic testing and symptomatology involving radicular or chest wall pain. Only patients who had failed conservative management, including physical therapy, chiropractic manipulation, exercises, drug therapy, and bedrest were included.

Inclusion criteria were a diagnosis of thoracic facet joint pain by means of controlled comparative local anesthetic blocks; patients who were over 18 years of age; patients with a history of chronic function-limiting thoracic pain of at least 6 months duration; and patients who are competent to understand the study protocol and provide voluntary, written informed consent and participate in outcome measurements.

Exclusion Criteria

Exclusion criteria were a lack of positive response to controlled comparative local anesthetic blocks, uncontrollable or unstable opioid use, uncontrolled psychiatric disorders, uncontrolled medical illness either acute or chronic, any conditions that could interfere with the interpretation of the outcome assessments, positioning, women who are pregnant or lactating, and patients with a history or potential for adverse reaction(s) to local anesthetic or steroid.

Pre-enrollment Evaluation

All patients understood and signed the IRB-approved protocol and the informed consent which described in detail all aspects of the study and withdrawal process. The informed consent also described potential side effects.

The diagnosis of facet joint pain was performed by controlled comparative local anesthetic blocks in

accordance with criteria established by IASP. Additional collected information included demographic data, medical and surgical history, radiologic investigations, physical examination, pain rating scores using the Numeric Rating Scale (NRS), work status, opioid intake, and functional status assessment by Oswestry Disability Index 2.0 (ODI).

Interventions*Diagnostic Facet Joint Nerve Blocks*

The diagnosis of facet joint pain was made by controlled comparative local anesthetic blocks in all patients, in accordance with IASP criteria (14). All thoracic facet joint nerve blocks were performed in a sterile operating room in an ambulatory surgery center, under fluoroscopy with a 22-gauge, 2" spinal needle. Controlled comparative facet joint nerve blocks were evaluated with a diagnostic process starting with diagnostic facet joint nerve blocks using 0.5 mL of 1% preservative-free lidocaine. Patients with a positive response to lidocaine were studied using 0.5 mL of 0.25% preservative-free bupivacaine on separate occasions, usually 3–4 weeks after the first injection. Target joints were identified by the pain pattern, local or paramedian tenderness over the area of the facet joints, and reproduction of the pain with deep pressure. Medial branch blocks were performed from C8 to T12 levels based on the clinical evaluation. Mild sedation with midazolam was provided. Each joint was blocked with at least 2 medial branch blocks. If the T3/4 facet joint was suspected to be involved, medial branch blocks were carried out at T2 and T3 levels; whereas if the T12/L1 facet joint was suspected to be involved T11 and T12 medial branch blocks were carried out. A positive response was considered when a patient reported at least an 80% reduction of pain assessed by a NRS and the ability to perform previously painful movements with continued relief of at least 80%. In addition, a positive response was only considered if the pain relief lasted at least 2 hours following the lidocaine injection and lasted at least 3 hours or greater than the duration of relief with lidocaine when bupivacaine was used; all other responses were considered as negative.

The facet joint nerve blocks were performed on the ipsilateral side in patients with unilateral pain, and bilateral facet joint nerve blocks were performed if patients had only axial pain or bilateral pain. Each nerve was injected with 0.5 to 1.0 mL of the assigned mixture and the blocks were performed on a mini-

mum of 2 nerves to block a single joint and 3 nerves on 2 consecutive joints.

Therapeutic Facet Joint Nerve Blocks

Therapeutic facet joint nerve blocks were performed at the same levels as the diagnostic facet joint nerve blocks which led to the inclusion into the study utilizing solutions as assigned into Group I or Group II with or without steroids. All therapeutic facet joint nerve blocks were performed with a 22-gauge, 2" spinal needle with injection of a 0.5 to 1 mL mixture in a sterile setting in the operating room under fluoroscopy. Repeat medial branch blocks were provided based on the response to prior therapeutic facet joint nerve blocks evaluated by improvement in pain and function in conjunction with deterioration in pain relief or functional status

Medial branch blocks were provided based on their responses. Protocol allowed the assigned treatments except in patients who were unblinded. Either the assigned treatment or another treatment based on their responses was provided to unblinded patients. The patients who were nonresponsive and in situations where medial branch blocks were stopped and other treatments were provided, these patients were considered to be withdrawn from the study, and no subsequent data were collected.

Co-interventions

New or specific co-interventions such as physical therapy, occupational therapy, or bracing were not offered during this treatment. However, the same co-interventions as scheduled including physical therapy and exercise program along with opioid and non-opioid analgesics, adjuvant analgesics were continued in all patients as necessary. Adjustments were also made as needed in medical therapy based on physical and functional status and continued response.

Additional Interventions

Patients were provided with assigned treatments in Group I and Group II. Protocol also allowed additional co-interventions if indicated including medial branch blocks.

Objective

The study was designed to evaluate the effectiveness of therapeutic thoracic medial branch blocks in managing chronic upper and mid back pain and to compare the role of a steroid in providing effective, function-improving, and long-lasting pain relief.

Outcomes

Outcomes measured included NRS, the ODI, employment status, and opioid intake. Assessment was carried out at 3 months, 6 months, and 12 months post-treatment.

NRS represented 0 with no pain and 10 with the worst pain imaginable. ODI was utilized for functional assessment though not evaluated for thoracic pain, the value and validity of the ODI has been reported (36). The reported thresholds for the minimum clinical important difference for ODI has been highly variable ranging from 4 to 15 points of change of a total score of 50. Thus, significant pain relief was described as 50% or more relief, whereas significant improvement in function was described as at least a 40% reduction of ODI.

Opioid intake was monitored as an outcome parameter. Opioid intake was determined as none, mild, moderate, or heavy, based on the dosage frequency and schedule of the drug. Heavy opioid intake was considered as the intake of any Schedule II opioids (i.e. oxycodone, morphine, meperidine, methadone, and transdermal fentanyl, in any dosage). Moderate opioid intake was considered as the intake of Schedule III opioids (hydrocodone up to 4 times a day). Mild opioid intake was considered as the intake of Schedule IV opioids (propoxyphene, pentazocine, and tramadol up to a maximum of 4 times or hydrocodone twice a day or less).

Employment and work status were determined based on employability of each patient, thus the data was analyzed as employable and non-employable persons. Those patients who were employed on a part-time basis due to pain were classified as employable; however, if the patients status of not being employed was secondary to being a housewife with no desire to return to work, retired, or over the age of 65, they were all considered in the non-employable category.

Sample Size

A sample size of a minimum of 30 patients was chosen for each group with a potential sample size of 50 for each group. The estimated sample size was based on previous studies of cervical (33) and lumbar medial branch neurotomies (37), which included less than 20 patients in each group. Further, other literature of interventional techniques identified 50 patients as acceptable (38).

Randomization/Sequence Generation

A total of 100 patients are expected to be randomized with 50 patients into each group. Computer-generated random allocations sequence concealment was utilized.

Allocation Concealment

Concealment was achieved by providing randomization by one of the 3 study coordinators.

Implementation

All the eligible patients were invited to enroll in the study if they met inclusion criteria.

Blinding

The random allocation was not revealed to personnel in the recovery room or to the physician performing the procedure.

Patients were unblinded if they requested to be unblinded or after completing 24 months of the study. Further, patients were also provided with an opportunity to discontinue or withdraw from the study for lack of pain relief, for lack of interest, or for any other reason. Patients were considered to be withdrawn if follow-up was lost.

For this evaluation and one-year follow-up report, all the patients completing the evaluation of 24 months (those unblinded), and the remaining patients were included with data being obtained by the statistician without unblinding. Thus, the randomization and double-blind nature of the study were preserved.

Statistical Methods

Statistical analysis included chi-squared statistic, Fisher's exact test, paired t-test, student t-test.

Chi-squared statistic was used to test the differences in proportions. A paired t-test was used to compare the pre- and post-treatment results of average pain scores and ODI measurements at baseline versus 3 months, 6 months, and 12 months. For comparison of mean scores between groups t-test was performed. Fisher's exact test was used wherever the expected value was less than 5.

Intent-to-treat-analysis

An intent-to-treat-analysis was performed. Either the last follow-up data or initial data were utilized in the patients who dropped out of the study and no other data were available.

RESULTS

Participant Flow

Figure 1 illustrates the participant flow.

Recruitment

The recruitment period continues at the present time. The recruitment started in May 2003. A total of 48 patients were enrolled, with 24 patients in each group by April 2007.

Baseline Data

Demographic characteristics are illustrated in Table 1. There were no significant differences noted among both groups.

The number of joints was as follows: 2 joints were involved in 23% of the patients, 3 joints were involved in 40% of the patients, 4 joints were involved in 17% of the patients and 5 joints were involved in 21% of the patients. Bilateral involvement was seen in 69% of the patients.

Analysis of Data

Patient flow is illustrated in Figure 1. The study period for one-year follow-up lasted from May 2003 to April 2008 with completion of one-year follow-up for all the patients included in the analysis. The data were available in the majority of patients. Intent-to-treat analysis was performed due to non-available data on 3 occasions in Group I and on 2 occasions in Group II.

Outcomes

Table 2 and Figure 2 illustrate the numeric pain scale scores at baseline, 3 months, 6 months, and 12 months. Pain scores changed significantly from baseline, and at 3 months, 6 months, and 12 months in both groups, with no significant differences between the groups or follow-up periods.

Figure 3 illustrates proportion of patients with significant pain relief of 50% or greater at 3 months, 6 months, and 12 months: 96%, 96%, 92% of the patients in Group I obtained significant pain relief, compared to Group II with 92%, 92%, 88% relief at 3, 6, and 12 months. There were no significant differences noted between groups, or from the 6-month and 12-month outcomes.

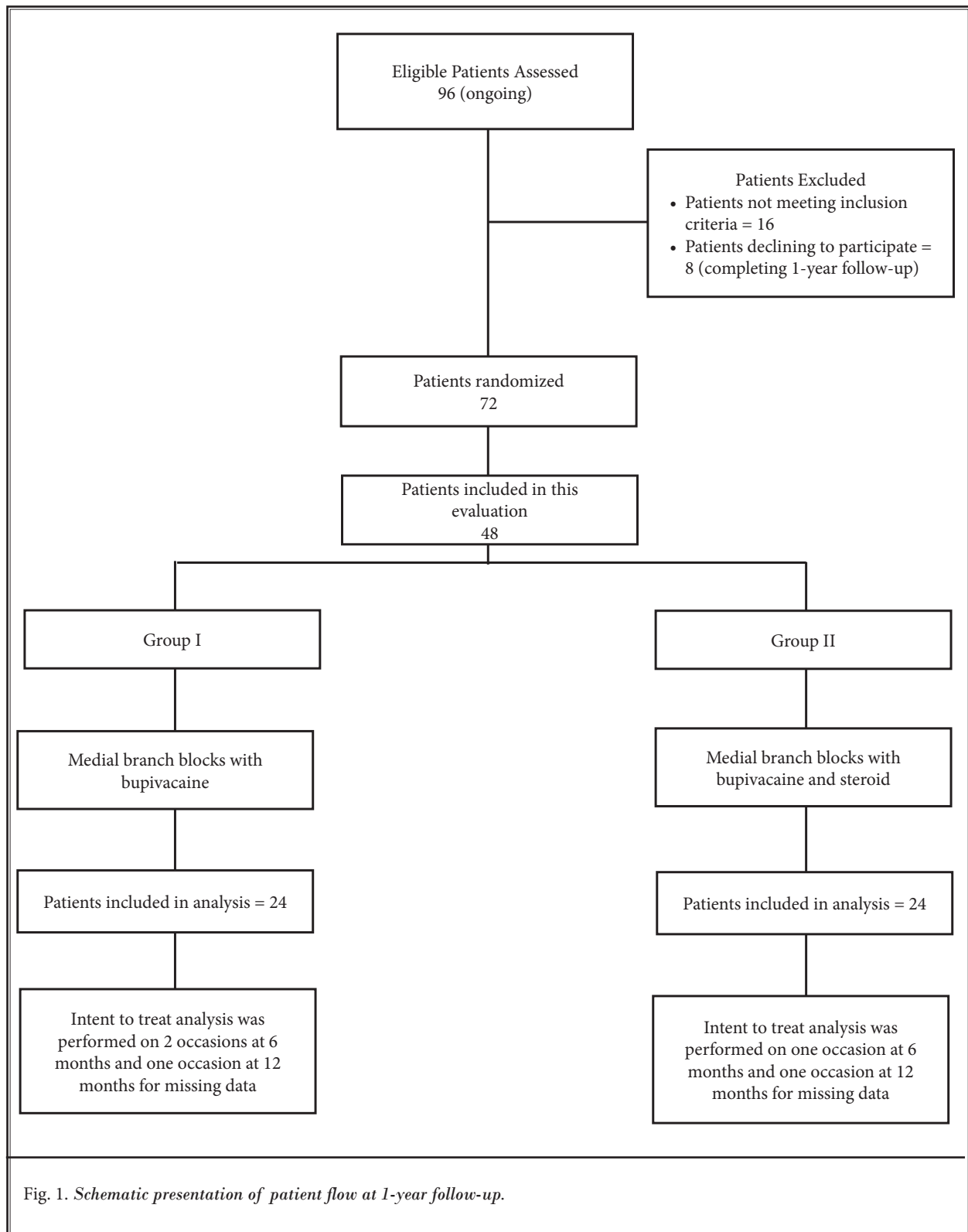


Table 1. Demographic characteristics

		Group I (N = 24)	Group II (N = 24)	P value
Gender	Male	46% (11)	42% (10)	1.000
	Female	54% (13)	58% (14)	
Age	Mean ± SD	47 ± 12.2	42 ± 11.6	0.128
Height (inches)	Mean ± SD	68 ± 3.6	67 ± 4.1	0.624
Weight (lbs.)	Mean ± SD	183 ± 43	181 ± 40	0.866
Duration of Pain (months)	Mean ± SD	75 ± 72	66 ± 65	0.666
Mode of onset of pain	Gradual	71% (17)	63% (15)	0.760
	Following incident	29% (7)	27% (9)	
H/O of previous thoracic surgery		4% (1)	4% (1)	1.000

Group I = bupivacaine only

Group II = bupivacaine and steroid

Table 2. Pain relief characteristics.

		Group I (N = 24)	Group II (N = 24)	P value
Average pain scores (Mean ± SD)	Baseline	7.6 ± 0.85	7.7 ± 1.23	0.892
	3 months	3.0 ± 0.75	3.0 ± 0.81	0.713
	6 months	2.9 ± 0.88	3.0 ± 0.91	0.631
	12 months	3.1 ± 0.88	3.0 ± 1.12	0.887

Group I = bupivacaine only

Group II = bupivacaine and steroid

The number of procedures performed per one year is illustrated in Table 3. The average number procedure performed in a year was 3.3 ± 0.95 and there was no significant differences noted between the groups.

Average pain relief per procedure is illustrated in Table 3. Average relief per procedure ranged from 16.8 ± 9.2 weeks in Group I and 15.3 ± 4.6 weeks in Group II with no significant difference. Therapeutic procedural characteristics with average total relief over a period of one-year are also illustrated in Table 3 with an average total pain relief of 50 ± 4.8 weeks and 46 ± 8.3 weeks in Group I and II respectively. Figure 3 illustrates proportion of patients with significant pain relief with 96% and 92% at 3 month and at 6 months; and 92% and 88% at 12 months in Groups I and II.

Functional Assessment

The evaluation by ODI provided the results of functional assessment. These results are illustrated in Table 4 and Figure 4. Significant improvement was demonstrated in the functional status in both groups from their baseline to one-year. Reduction of ODI scores of at least 40% was seen in 88% of the patients in Group I and Group II, whereas, a 50% reduction was seen in 79% of the patients in Group I and 75% in Group II at 1 year from baseline.

Employment Characteristics

The employment characteristics are illustrated in Table 5. Employment was evaluated based on employability. At baseline, there were 11 patients employable

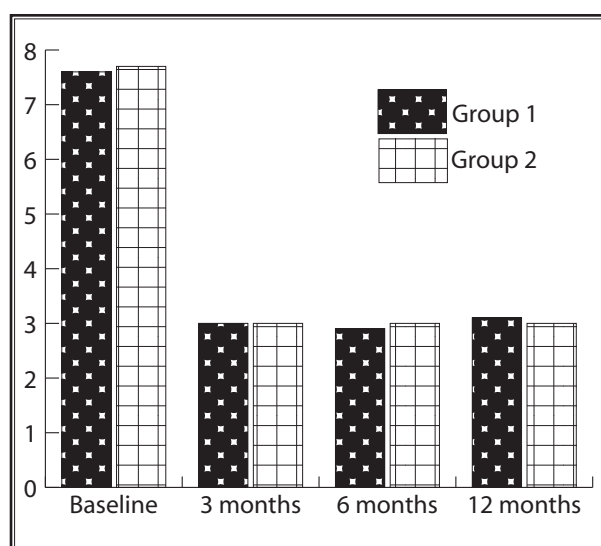
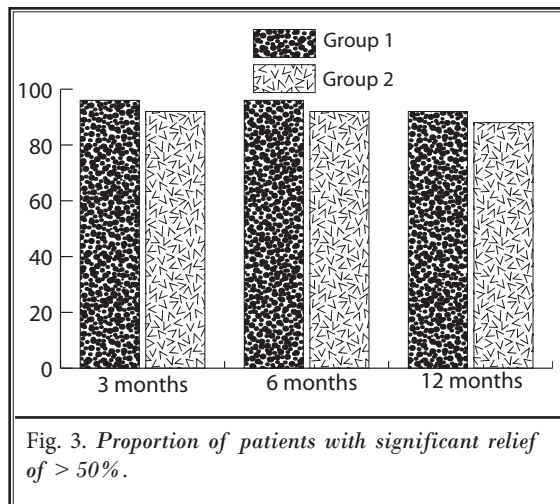


Fig. 2. Pain relief characteristics.

Table 3. Therapeutic procedural characteristics with procedural frequency, average relief per procedure, and average total relief in weeks over a period of 1 year.

Number of Procedures	Group I (bupivacaine only) (N = 24)			Group II (bupivacaine and steroid) (N = 24)		
	Procedural frequency	Average relief per procedure (weeks)	Average total relief (weeks)	Procedural frequency	Average relief per procedure (weeks)	Average Total relief (weeks)
One	4% (1)	52 (1)	52 (1)	4% (1)	26 (1)	26 (1)
Two	17% (4)	26 ± 0 (4)	52 ± 0 (4)	17% (4)	20.6 ± 7.1 (4)	41 ± 14.2 (4)
Three	21% (5)	15.6 ± 2.4 (5)	47 ± 7.1 (5)	33% (8)	15.0 ± 1.9 (8)	45 ± 5.6 (8)
Four	50% (12)	12.4 ± 1.2 (12)	50 ± 4.8 (12)	46% (11)	12.5 ± 0.7 (11)	50 ± 2.8 (11)
Five	8% (2)	9.9 ± 0.7 (2)	50 ± 3.6 (2)	0%	-	-
Average data	3.4 ± 1.02	16.8 ± 9.2	50 ± 4.8 (24)	3.2 ± 0.88	15.3 ± 4.6	46 ± 8.3 (24)



in Group I and of these, 8 were employed and 3 unemployed, whereas in Group II, there were 8 employable and 7 were employed at baseline. At one-year follow-up, there were 11 employed in Group I and 10 employed in Group II.

Opioid Intake

The majority of the patients at baseline, as well as at 12 months, received moderate doses of opioids. However, there were no significant differences noted between the groups.

Adverse Events

There were no major adverse events reported over a period of one-year in 48 patients.

Table 4. Functional assessment evaluated by Oswestry Disability Index.

		Group I (N = 24)	Group II (N = 24)	P value
Disability Scores (Mean ± SD)	Baseline	23.8 ± 6.9	25.5 ± 5.6	0.351
	3 months	11.5* ± 5.2	10.6* ± 4.4	0.513
	6 months	11.2* ± 4.9	10.6* ± 4.4	0.668
	12 months	10.5* ± 4.0	10.9* ± 4.5	0.712

*indicates significant difference with baseline

Group I = bupivacaine only
Group II = bupivacaine and steroid

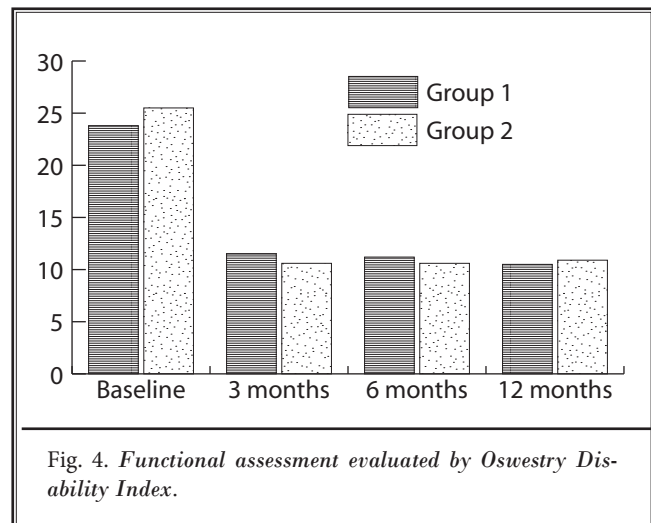


Table 5. *Employment characteristics.*

Employment status	Group I		Group II	
	Baseline	12 months	Baseline	12 months
Employed part-time	1	3	0	2
Employed full-time	7	8	7	8
Unemployed due to pain	2	1	1	0
Unemployed - Student	1	0	0	0
Total Employed	8	11	7	10
Eligible for employment	11	11	8	8
Housewife	1	0	2	1
Disabled	9	9	14	13
Over 65 year of age	3	3	0	0
Total Number of Patients	24	24	24	24

DISCUSSION

This randomized, double-blind trial, of 48 patients undergoing therapeutic thoracic medial branch nerve blocks, with chronic, function-limiting mid back or upper back pain secondary to thoracic facet joint involvement showed significant improvement with decreased pain and improved functional status. Significant pain relief of 50% or greater of varying duration was seen in 92% of patients in Group I and 88% of patients in Group II with no significant differences noted with or without steroids over a period of one-year. Functional assessment measured by ODI also showed significant improvement with at least a 50% reduction of disability scores in 79% of patients in Group I and 75% of patients in Group II over a period of one-year. Further, at least 40% reduction in disability scores was noted in 88% of patients in Group I and 88% of patients in Group II over a period of one-year. Combined > 50% pain relief and > 40% improvement in ODI scores was seen in 79%-83% of patients. The average pain relief per procedure ranged from 10 to 52 weeks and patients experienced 46 to 50 weeks of significant pain relief during one-year. Clinically important improvement was noted with employment status even though there was no significant difference noted. There was no change in opioid intake.

There were no randomized, double-blind trials performed to evaluate the effects of thoracic facet joint pain in the past. A prospective study (27) reported results of 55 consecutive patients meeting the diag-

nostic criteria of thoracic facet joint pain by means of comparative, controlled diagnostic blocks. The results showed significant improvement with pain relief and reduction (50%) with ODI scores in 71% of the patients at 3 months and 6 months, 77% at 12 months, compared to baseline measurements. The results of this study are comparable to the prospective evaluation.

The limitations of this study include a lack of placebo group, a small number of patients, and a lack of hypothesis to illustrate the effectiveness of medial branch blocks with or without steroids. The lack of a placebo group is a shortcoming of the study even though issues of ethics, feasibility, and cost pose challenges to the inclusion of a placebo group in the United States for interventions. However, in modern medicine, the practical clinical trials (39) measuring effectiveness are considered more appropriate than explanatory trials measuring efficacy (40). Considering that practical trials are best designed to provide the results of the benefit of treatments produced in routine clinical practice and also to address questions about the risks, benefits, and costs of an intervention as they occur in routine clinical practice better than explanatory trial, the design of the study is considered as appropriate. In practical clinical trials, without a placebo group, with a pragmatic approach, the treatment response is the combination of the treatment effect and placebo effect, as this will best reflect the likely clinical response in actual practice.

The small number of patients with 24 patients in each group is not a major limitation in the present study. Multiple techniques are used in sample size determination and power calculations are carried out. However, in interventional pain management techniques the number of patients enrolled are generally less than 20 (33,37) and a high quality study is considered with at least 50 patients (38). Considering the paucity of literature on thoracic medial branch blocks specifically, and in thoracic pain in general we consider it is important to provide the results of this study to researchers, systematic reviewers, practitioners, and patients. Further, there was no significant difference in this study with medial branch blocks compared to the previous thoracic medial branch blocks prospective study (27) and other randomized double-blind trials evaluating the effectiveness of medial branch blocks in the cervical and lumbar spine (29-32).

Finally, even though we have shown there was no significant difference between the groups receiving either bupivacaine alone or bupivacaine with non-particulate betamethasone, we have not provided a hypothesis. The lack of significant differences between the patients receiving medial branch blocks with or without steroids is similar to the previous controlled trials of medial branch blocks (29-32).

The effect of local anesthetics and steroids in providing long-term relief continues to be an enigma. The basis for intraarticular injection has been that there is inflammation and steroids are used to treat the inflammation. No such claims have been made with facet joint nerve blocks. The present study shows a lack of support for the theory of inflammation and also a lack of role of steroids in thoracic medial branch blocks, similar to lumbar and cervical medial branch blocks (29,32). Thus, facet joint pain may be related to not only a nociceptive component, but also a neuropathic component (41,42). Shah and Kaye (41) reported facet joint pain especially in the cervical spine, being arguably neuropathic rather than nociceptive. In fact, Freynhagen et al (42) attempted to assess whether pseudoradicular low-back pain might be associated with subclinical sensory deficits in the distal extremity by application of quantitative sensory testing protocol in patients with pseudoradicular pain distribution. They described that the rationale between the distinction between radicular and pseudoradicular pain stems from the assumption that neuropathic versus nociceptive pain types differ in their underlying pain generating mechanisms. In

pseudoradicular low back pain a proximal nociceptive event like mechanical factor, musculoskeletal dysfunctions, degenerative changes in connective tissues, and local or even systemic inflammation are regarded to lead to a referred sensation in proximately dermatomes of the leg - a nociceptive component. In contrast, compression or damage to a nerve root by a protruded intervertebral disc or an inflammatory etiology are suspected to be the main causes of radicular pain which is therefore categorized as pain with a neuropathic component. In this study, they demonstrated subclinical sensory deficits in the pseudoradicular low-back pain group by quantitative sensory testing, raising the question, whether it is really appropriate to draw a clear line between radicular and pseudoradicular patients, or whether pseudoradicular syndromes indicate a milder degree of nerve root damage by not affecting all nerve fibers in the root, with a neuropathic component.

Epidural corticosteroids have been postulated to provide a certain level of efficacy by their anti-inflammatory, immunosuppressive, anti-edema effects, and inhibition of neurotransmission within the C-fibers (43-46). In contrast, local anesthetics have been described to provide short-term symptomatic relief. Thus, with lack of explanation for the mechanism of relief of local anesthetics on a long-term basis (47-49). However, postulations explain that the effectiveness of local anesthetics may be related to the direct effects of the local anesthetic on various mechanisms in chronic pain (47-49). Consequently, the pathophysiologic mechanisms that form the basis for chronic pain not only include the presence of noxious peripheral stimulation, but also excess nociception resulting in the sensitization of the pain pathways at several neuronal levels (48,49), and excess release of neurotransmitters causing complex central responses including hyperalgesia or windup (47). Thus, all the responses of chronic pain mechanisms may result in an increase in nociceptive sensitization of the nervous system (50,51), and phenotype changes which are also considered as part of neuronal plasticity (50-52). Further, all these mechanisms provide similar aspects to neuropathic pain (50,51,53). Paradoxically, corticosteroids are not effective in neuropathic pain, whereas local anesthetics have been shown to be effective in the management of neuropathic pain (54), including the prevention of onset and the treatment of phantom-limb syndrome (49,55,56). Consequently, it is postulated that local anesthetics provide relief

by suppression of nociceptive discharge (57), the block of the axonal transport (58,59), the block of the sympathetic reflex arc (44,54), the block of sensitization (48,49), anti-inflammatory effect (60,61), and blockade of axonal transport of nerve fibers at lower concentrations compared with those that are necessary for a block of a nerve conduction (58,59). The long-lasting effect of local anesthetics on nerve blocks and epidural injections has been demonstrated in multitude of previous studies, since 1941 (27,29,32,57,62-73).

Since the early descriptions in 1941 reporting that the analgesic effect of a 2% procaine injection may continue for 4 to 6 weeks (62), multiple investigators have provided evidence for the same, with effective use of these properties in achieving pain relief beyond the expected duration of local anesthetics after a series of blocks and sometimes even after a single block has been utilized. Recently, Sato et al (74) evaluated the prolonged analgesic effect of epidural ropivacaine in a rat model of neuropathic pain and concluded that repetitive administration of ropivacaine into the epidural space in rats exerts an analgesic effect, possibly by inducing a plastic change in nociceptive circuit.

Tachihara et al (75) evaluated whether corticosteroids produce additional benefit to nerve root infiltration for experimental lumbar disc herniation. In evaluation in rats, they showed nerve root infiltration prevented mechanical allodynia. However, no additional benefit from using corticosteroid was identified, suggesting that corticosteroid may be unnecessary for nerve root blocks. The local anesthetic therapeutic mechanism of nerve root infiltration was explained on the basis of the results of experimental investigation showing in the application of nucleus pulposus to the nerve root induces an increase in endoneural fluid pressure (EFP) and a decrease of blood flow in dorsal root ganglion (76). Increased pressure is caused by interference with capillary flow and intraneural edema, followed by a breakdown of the myelin sheath and other cytoplasmic components of Schwann cells and the axon (77,78). Lidocaine reportedly reduces the increase in EFP and pathophysiological changes in the dorsal root ganglion induced by nucleus pulposus (79). Further, lidocaine may influence intra-radicular blood flow and exert therapeutic effects by improving EFP and blood flow in the dorsal root ganglion (80). In addition, lidocaine has been postulated to decrease aci-

dosis by increasing blood flow (81) and interrupt the viscous cycle of pain by desensitizing the central and peripheral nervous systems by blocking abnormal impulses from and to the involved nerve root and DRG (82).

Corticosteroid anti-inflammatory properties have been described to relate to the inhibition of prostaglandin synthesis and decreases in regional levels or inflammatory mediators such as interleukin-1, tumor necrosis factor, and phospholipase A2 (45,83-85). Thus, corticosteroids have therapeutic effects on radicular symptoms caused by lumbar disc herniation due to their anti-inflammatory function. Furthermore, corticosteroids reportedly ameliorate early vascular permeability increases in spinal nerve roots and inhibit reductions in nerve conduction velocity induced by epidural application of nucleus pulposus (86). Finally, corticosteroids may exert "anesthetic-like" actions on nociceptive C-fiber conduction independent of anti-inflammatory properties (46). However, unlike local anesthetics, corticosteroids are known to possess direct neurotoxic effects on peripheral nerve tissue (87). Corticosteroids may have some detrimental effects on the function of macrophages, which are thought to play a role in the resorption of herniated intervertebral discs (88), dexamethasone reportedly causes reduced blood flow in normal nerves and dorsal root ganglion (89), and preservative and buffering agents also are neurotoxic (90).

The results described here are from a private practice, interventional pain management setting, in a practical and pragmatic clinical trial in the United States. The results are not applicable in the general population unless the same methodology is utilized with the diagnosis and therapy. Further, generalizability of the findings of this study may only be feasible in studies utilizing larger populations in multiple settings with longer term follow-up. Proper selection is essential specifically with controlled comparative local anesthetic blocks.

In summary, evidence in this report demonstrates thoracic facet joint pain diagnosed by controlled, comparative local anesthetic blocks with the criteria of 80% pain relief, which is sustained after prior painful movements for appropriate duration of action of local anesthetic, may be coupled with thoracic medial branch blocks with or without steroid providing approximately 46 to 50 weeks of relief and requiring 3 to 4 episodes of treatments per year.

CONCLUSION

The results of this randomized, double-blind, controlled evaluation of thoracic facet joint nerve blocks in chronic function-limiting upper back or mid back pain secondary to facet joint involvement demonstrate the effectiveness in over 88% of the patients with improvement in functional status.

ACKNOWLEDGMENTS

The authors wish to thank the Editorial Board of *Pain Physician* for review and criticism in improving the manuscript, and Tonie M. Hatton and Diane E. Neihoff, transcriptionists, for their assistance in preparation of this manuscript.

REFERENCES

- Manchikanti L, Schultz DM, Falco FJ, Singh V. Thoracic facet joint interventions. In Manchikanti L, Singh V (eds). *Interventional Techniques in Chronic Spinal Pain*, ASIPP Publishing, Paducah, KY, 2007; 277-294.
- Manchikanti L, Pampati VS. Research designs in interventional pain management: Is randomization superior, desirable or essential? *Pain Physician* 2002; 5:275-284.
- Stolker RJ, Vervest AC, Groen GJ. Percutaneous facet denervation in chronic thoracic spinal pain. *Acta Neurochir* 1993; 122:82-90.
- Linton SJ, Hellsing AL, Hallden K. A population based study of spinal pain among 35-45-year-old individuals. *Spine* 1998; 23:1457-1463.
- Wilson PR. Thoracic facet joint syndrome – a clinical entity? *Pain Suppl* 1987; 4:S87.
- Dreyfuss P, Tibiletti C, Dreyer SJ. Thoracic zygapophyseal joint pain patterns: A study in normal volunteers. *Spine* 1994; 19:807-811.
- Fukui S, Ohseto K, Shiotani M. Patterns of pain induced by distending the thoracic zygapophyseal joints. *Reg Anesth* 1997; 22:332-336.
- Manchikanti L, Singh V, Pampati VS, Beyer CD, Damron KS. Evaluation of the prevalence of facet joint pain in chronic thoracic pain. *Pain Physician* 2002; 5:354-359.
- Manchikanti L, Boswell MV, Singh V, Pampati VS, 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.
- 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.
- Seghal N, Dunbar EE, Shah RV, Colson JD. Systematic review of diagnostic utility of facet (zygapophysial) joint injections in chronic spinal pain: An update. *Pain Physician* 2007; 10:213-228.
- Boswell MV, Singh V, Staats PS, Hirsch JA. Accuracy of precision diagnostic blocks in the diagnosis of chronic spinal pain of facet or zygapophysial joint origin. *Pain Physician* 2003; 6:449-456.
- Seghal N, Shah RV, McKenzie-Brown A, Everett CR. Diagnostic utility of facet (zygapophysial) joint injections in chronic spinal pain: A systematic review of evidence. *Pain Physician* 2005; 8:211-224.
- Merskey H, Bogduk N. Classification of Chronic Pain. *Descriptions of Chronic Pain Syndromes and Definition of Pain Terms*, 2nd ed. International Association for the Study of Pain. IASP Press, Seattle, 1994.
- Bogduk N. Low back pain. *Clinical Anatomy of Lumbar Spine and Sacrum*, 4th edition. Churchill Livingstone, New York, 2005, pp 183-216.
- Stolker RJ, Vervest AC, Groen GJ. Parameters in electrode positioning in thoracic percutaneous facet denervation: An anatomical study. *Acta Neurochir* 1994; 128:32-39.
- Stolker RJ, Vervest AC, Groen GJ. The treatment of chronic thoracic segmental pain by radiofrequency percutaneous partial rhizotomy. *J Neurosurg* 1994; 80:986-992.
- Stolker RJ, Vervest AC, Ramos LM, Groen GJ. Electrode positioning in thoracic percutaneous partial rhizotomy: An anatomical study. *Pain* 1994; 57:241-251.
- Dreyfuss P, Tibiletti C, Dreyer S, Sobel J. Thoracic zygapophyseal pain: A review and description of an intraarticular block technique. *Pain Digest* 1994; 4:44-52.
- Chua WH, Bogduk N. The surgical anatomy of thoracic facet denervation. *Acta Neurochir* 1995; 136:140-144.
- Stolker RJ, Vervest AC, Groen GJ, De Ruiter JW, Hansen L. On the innervation of the dorsal compartment of the thoracic spine. In Stolker RJ, Vervest AC (eds). *Pain Management by Radiofrequency Procedures in the Cervical and Thoracic Spine: A Clinical and Anatomical Study*. Utrecht, Thesis, 1994, pp 133-144.
- Stilwell DL. The nerve supply of the vertebral column and its associated structures in the monkey. *Anat Rec* 1956; 125:139-169.
- Bogduk N. International Spinal Injection Society guidelines for the performance of spinal injection procedures. Part 1: Zygapophyseal joint blocks. *Clin J Pain* 1997; 13:285-302.
- Boswell MV, Trescot AM, Datta S, Schultz DM, Hansen HC, Abdi S, Seghal N, Shah RV, Singh V, Benyamin RM, Patel VB, Buenaventura RM, Colson JD, Cordero HJ, Epter RS, Jasper JF, Dunbar EE, Atluri SL, Bowman RC, Deer TR, Hansen HC, 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.
- Boswell MV, Colson JD, Seghal N, Dunbar EE, Epter R. A systematic review of therapeutic facet joint interventions in chronic spinal pain. *Pain Physician* 2007; 10:229-254.
- Manchikanti L, Singh V, Vilims BD, Hansen HC, Schultz DM, Kloth DS. Medial branch neurotomy in management of chronic spinal pain: Systematic review of the evidence. *Pain Physician* 2002; 5:405-418.

27. 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.
28. Tzaan W, Tasker R. Percutaneous radiofrequency facet rhizotomy—experience with 118 procedures and reappraisal of its value. *Can J Neurol Sci* 2000; 27:125-130.
29. Manchikanti LM, Singh V, Falco FJE, Cash KM, Fellows B. Cervical medial branch blocks for chronic cervical facet joint pain: A randomized, double-blind, controlled trial with 1-year follow-up: Clinical Trial NCT0033272. *Spine* 2008; 33:1813-1820.
30. 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 NCT0033272. *Pain Physician* 2006; 9:333-346.
31. Manchikanti L, Manchikanti KN, Damron KS, Pampati V. Effectiveness of cervical medial branch blocks in chronic neck pain: A prospective outcome study. *Pain Physician* 2004; 7:195-201.
32. 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.
33. Lord SM, Barnsley L, Wallis BJ, McDonald GJ, Bogduk N. Percutaneous radiofrequency neurotomy for chronic cervical zygapophysial joint pain. *N Engl J Med* 1996; 335:1721-1726.
34. Barnsley L. Percutaneous radiofrequency neurotomy for chronic neck pain: Outcomes in a series of consecutive patients. *Pain Med* 2005; 6:282-286.
35. Moher D, Schulz KF, Altman D, for the CONSORT Group. The CONSORT statement: Revised recommendations for improving the quality of reports of parallel-group randomized trials. *JAMA* 2001; 285:1987-1991.
36. Fairbank JCT, Pynsent PB. The Oswestry Disability Index. *Spine* 2000; 25:2940-2953.
37. van Kleef M, Barendse GA, Kessels A, Voets HM, Weber WE, de Lange S. Randomized trial of radiofrequency lumbar facet denervation for chronic low back pain. *Spine* 1999; 24:1937-1942.
38. Koes BW, Scholten RJ, Mens JM, 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.
39. Roland M, Torgerson DJ. What are pragmatic trials? *BMJ* 1998; 316:285.
40. Tunis SR, Stryer DB, Clancy CM. Practical clinical trials. Increasing the value of clinical research for decision making in clinical and health policy. *JAMA* 2003; 290:1624-32.
41. Shah RV, Kaye AD. Evolving concepts in the understanding of cervical facet joint pain. *Pain Physician* 2004; 7:295-299.
42. Freynhagen R, Rolke R, Baron R, Tölle TR, Rutjes AK, Schu S, Treede RD. Pseudoradicular and radicular low-back pain - a disease continuum rather than different entities? Answers from quantitative sensory testing. *Pain* 2008; 135:65-74.
43. Grenier B, Castagnera L, Maurette P, Ery 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.
44. Hayashi N, Weinstein JN, Meller ST, Lee SM, 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.
45. 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.
46. Johansson A, Hao J, Sjolund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. *Acta Anaesthesiol Scand* 1990; 34:335-338.
47. Pasqualucci A, Varrassi G, Braschi A, Peduto VA, Brunelli A, Marinangeli F, Gori F, Colò F, Paladín 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.
48. Katz WA, Rothenberg R. The nature of pain: Pathophysiology. *J Clin Rheumatol* 2005; 11(2 suppl):S11-15.
49. Melzack R,Coderre TJ, Katz J, Vaccarino AL. Central neuroplasticity and pathological pain. *Ann N Y Acad Sci* 2001; 933:157-174.
50. 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.
51. Decosterd I, Woolf CJ. Spared nerve injury: An animal model of persistent peripheral neuropathic pain. *Pain* 2000; 87:149-158.
52. Pennypacker KR, Hong JS, McMillian MK. Implications of prolonged expression of Fos-related antigens. *Trends Pharmacol Sci* 1995; 16:317-321.
53. Ji RR, Woolf CJ. Neuronal plasticity and signal transduction in nociceptive neurons: Implications for the initiation and maintenance of pathological pain. *Neurobiol Dis* 2001; 8:1-10.
54. Mao J, Chen LL. Systemic lidocaine for neuropathic pain relief. *Pain* 2000; 87:7-17.
55. Pasqualucci A. Experimental and clinical studies about the preemptive analgesia with local anesthetics. Possible reasons of the failure. *Minerva Anestesiol* 1998; 64:445-457.
56. 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.
57. 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.
58. Lavoie PA, Khazen T, Filion PR. Mechanisms of the inhibition of fast axonal transport by local anesthetics. *Neuropharmacology* 1989; 28:175-181.
59. Bisby MA. Inhibition of axonal transport in nerves chronically treated with local anesthetics. *Exp Neurol* 1975; 47:481-489.
60. Benzon HT. Epidural steroid injections for low back pain and lumbosacral radiculopathy. *Pain* 1986; 24:277-295.
61. Cassuto J, Sinclair R, Bonderovic M. Anti-inflammatory properties of local

- anesthetics and their present and potential clinical implications. *Acta Anaesthesiol Scand* 2006; 50:265-282.
62. Wertheim HM, Rovenstine EA. Suprascapular nerve block. *Anesthesiology* 1941; 2:541.
 63. 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 follow-up. *J Bone Joint Surg Am* 2006; 88:1722-1725.
 64. Riew KD, Yin Y, Gilula L, Bridwell KH, Lente LG, Laurysen C, Goette K. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. A prospective, randomized, controlled, double-blind study. *J Bone Joint Surg Am* 2000; 82-A:1589-1593.
 65. 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.
 66. Bonica JJ. *The Management of Pain*. Lea and Febiger, Philadelphia, 1963.
 67. 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.
 68. Livingston WK. *Pain Mechanisms*. Macmillan, New York, 1943.
 69. Raj PP. Prognostic and therapeutic local anaesthetic blockade. In Cousins MJ, Bridenbaugh PO (eds). *Neural Blockade*. Lippincott, Philadelphia, 1988, pp 900-901.
 70. Kibler RF, Nathan PW. Relief of pain and paraesthesiae by nerve block distal to a lesion. *J Neurol Neurosurg Psychiatr* 1960; 23:91-98.
 71. Xavier AV, McDanal J, Kissin I. Relief of sciatic radicular pain by sciatic nerve block. *Anesth Analg* 1988; 67:1177-1180.
 72. Manchikanti L, Pampati V, Fellows B, Bakhit CE. The diagnostic validity and therapeutic value of lumbar facet joint nerve blocks with or without adjuvant agents. *Curr Rev Pain* 2000; 4:337-344.
 73. Manchikanti KN, Pampati V, Dameron KS, McManus CD. A double-blind, controlled evaluation of the value of Sarapin in neural blockade. *Pain Physician* 2004; 7:59-62.
 74. 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.
 75. 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.
 76. 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.
 77. Myers RR, Mizisin AP, Powell HC, Lampert PW. Reduced nerve blood flow in hexachlorophene neuropathy. *J Neuro-path Exp Neurol* 1982; 41:391-399.
 78. Myers RR, Powell Hc, Costello ML, Lampert PW, Zweifach BW. Endoneurial fluid pressure: Direct measurement with micropipettes. *Brain Res* 1978; 148:510-515.
 79. Onda A, Yabuki S, Kikuchi S, Satoh K, Myers RR. Effects of lidocaine on blood flow and endoneurial fluid pressure in a rat model of herniated nucleus pulposus. *Spine* 2001; 26:2186-2191.
 80. Yabuki S, Kikuchi S. Nerve root infiltration and sympathetic block: An experimental study of intraradicular blood flow. *Spine* 1995; 20:901-906.
 81. Ohtori S, Inoue G, Koshi T, Ito T, Doya H, Saito T, Moriya H, Takahashi K. Up-regulation of acid-sensing ion channel 3 in dorsal root ganglion neurons following application of nucleus pulposus on nerve root in rats. *Spine* 2006; 31:2048-2052.
 82. Hasue M. Pain and the nerve root. *Spine* 1993; 18:2053-2058.
 83. Bendrups A, Hilton A, Meager A, Hamilton JA. Reduction of tumor necrosis factor alpha and interleukin-1 beta levels in human synovial tissue by interleukin-4 and glucocorticoid. *Rheumatol Int* 1993; 12:217-220.
 84. Kantrowitz F, Robinson DR, McGuire MDB. Corticosteroids inhibit prostaglandin production by rheumatoid synovia. *Nature* 1975; 258:737.
 85. Saal JS, Franson RC, Dobrow R, Saal JA, White AH, Goldthwaite N. High levels of inflammatory phospholipase A2 activity in lumbar disc herniations. *Spine* 1990; 15:674-678.
 86. Byrod G, Otani K, Brisby H, Rydevik B, Olmarker K. Methylprednisolone reduces the early vascular permeability increases in spinal nerve roots induced by epidural nucleus application. *J Orthop Res* 2000; 18:983-987.
 87. Mackinnon SE, Hudson AR, Gentili F, Kline DG, Hunter D. Peripheral nerve injection injury with steroid agents. *Plast Reconstr Surg* 1982; 69:482-489.
 88. Minamide A, Tamaki T, Hashizume H, Yoshida M, Kawakami M, Hayashi N. Effects of steroid and lipopolysaccharide on spontaneous resorption of herniated intervertebral discs: An experimental study in the rabbit. *Spine* 1998; 23:870-876.
 89. Shishido H, Kikuchi S, Heckman H, Myers RR. Dexamethasone decreases blood flow in normal nerves and dorsal root ganglia. *Spine* 2002; 27:581-586.
 90. Manchikanti L. Pharmacology of neuraxial steroids. In Manchikanti L, Singh V (eds). *Interventional Techniques in Chronic Spinal Pain*, ASIPP Publishing, Paducah, KY, 2007; 167-184.