Spinal Manipulation Postepidural Injection for Lumbar and Cervical Radiculopathy: A Retrospective Case Series

Paul Dougherty, DC,[a] Saeed Bajwa, MD,[b] Jeanmarie Burke, PhD,[a] and J. Donald Dishman, DC[a]

Abstract

Objective: To describe the safety and potential therapeutic benefit of spinal manipulation postepidural injection in the nonsurgical treatment of patients with cervical and lumbar radiculopathy.

Methods: The study design was a retrospective review of outcomes of 20 cervical and 60 lumbar radiculopathy patients who underwent spinal manipulation postepidural injection in a hospital setting. Patients received either fluoroscopically guided or computed tomography (CT)–guided epidural injection of a combination of lidocaine and Depo-Medrol. The manual therapy consisted of an immediate postepidural application of flexion distraction mobilization and then high-velocity, low-amplitude spinal manipulation to the affected spinal regions. Outcome criteria were empirically defined as significant improvement, temporary improvement, or no change. The minimum follow-up time for all patients was 1 year.

Results: There were no complications associated with spinal manipulation, whereas 3 complications associated with the epidural injection procedure were noted. Of lumbar spine patients, 36.67% (n = 22) noted significant improvement, 41.67% (n = 25) experienced temporary improvement, and 21.67% (n = 13) reported no change. Of the patients undergoing spinal manipulation after cervical epidural injection, 50% (n = 10) noted significant improvement, 30% (n = 6) experienced temporary improvement, whereas 20% (n = 4) exhibited no change.

Conclusions: These data suggest that spinal manipulation postepidural injection is a safe nonsurgical procedure to use in the treatment of the patient with radiculopathy of spinal origin. This is also the first report of the use of spinal manipulation postepidural injection in the cervical spine. (J Manipulative Physiol Ther 2004;27:449-56)

Key Indexing Terms: *Radiculopathy; Spinal Manipulation; Epidural Steroid Injections*

Introduction

The multifactorial cause of spinal and radicular pain has long remained a challenge for the clinician. Decompression and fusion procedures have been longstanding standards of care for the patient with herniated nucleus pulposus (HNP). However, magnetic resonance imaging (MRI) studies detect many asymptomatic disk herniations.[1-3] Patients with seemingly insignificant annular tears can exhibit back pain that does not appear to correlate with the level of severity of the lesion.[4-6] Some patients with annular tears exhibit radicular pain consistent with radiculopathy despite the lack of imaging evidence of nerve root encroachment.[7]

Current models of radicular pain describe the multifactorial nature of the disorder by implicating the mechanical, vascular, inflammatory, and neural components. The mechanical lesions may initiate circulatory changes and/or inflammatory responses.[8-12] Ischemia caused by compression can evoke spontaneous ectopic firing and increase the mechanical sensitivity of the dorsal root ganglia (DRG).[13] The enzymatic activity involved in the inflammatory process is reported to be capable of inducing neurotoxic changes, especially to the DRG.[14] Chronic nociceptive input may lead to an enhanced responsiveness of the central nervous system to afferent input. This response reportedly creates decreased thresholds to nociceptive stimuli, as well as sustained neural activity of dorsal horn neurons after the stimulus has been terminated.[15] This neuroplastic phenomenon has been termed *central sensitization*.[16] As such, any therapeutic regimen must address

[a]New York Chiropractic College, Seneca Falls, NY.
[b]Southern New York Neurosurgical Group, P.C., Hospital Affiliation, United Health Services Hospitals, Johnson City, NY.
Submit requests for reprints to: Paul E. Dougherty, DC, New York Chiropractic College, 2360 SR 89, Seneca Falls, NY 13148 (e-mail: *pdougherty@nycc.edu*).
Paper submitted March 17, 2003; in revised form March 3, 2003.
0161-4754/$30.00

doi:10.1016/j.jmpt.2004.06.003

the contributions of mechanical, vascular, inflammatory, and neural mechanisms to the pathogenesis of the radicular pain syndrome.

Conservative medical procedures for treating radicular pain syndromes involve epidural injections of steroids with or without the use of an anesthetic. The clinical rationale of this procedure is to introduce a local dosage of a corticosteroid, which theoretically leads to a reduction in perineural inflammation.[17] These effects are produced as a result of corticosteroid inhibition of specific leukocyte functions, including aggregation at inflammatory sites; prevention of degranulation of granulocytes, mast cells, and macrophages; and stabilization of lysosomal and other membranes.[18] Injections of local anesthetics, such as lidocaine, may interrupt the neural activity that produces and perpetuates the pain syndrome and also relax the paraspinal muscle spasm.[19] Local anesthetics reversibly block impulse conduction along nerve axons and other excitable membranes that use sodium channels as the primary means of action potential generation.[19] Epidural steroid injection (ESI), for the purpose of this article, will be defined as an injection of steroid agents alone, whereas ESI with anesthetics will refer to an injection of steroid agents with the use of an anesthetic.

A recent systematic review of the literature indicated that ESI may be beneficial for nerve root compression.[20] The evidence from randomized controlled trials on the efficacy of ESI for subacute and chronic low back pain is not convincing,[19] despite having moderate evidence-based support from a large-scale prospective case series.[21] ESIs have also been shown to be safe and effective in the treatment of the neck and arm.[21] However, randomized controlled trials on ESI for neck pain and arm pain are lacking.

Spinal manipulation is also a commonly used therapeutic regime for patients with pain of spinal origin. The clinical rationale for the use of spinal manipulation is to increase the range of motion of the functional spinal unit and also to modulate sensory input to the central nervous system.[22-25] Recent systematic reviews of the literature have found that spinal manipulation is likely to be beneficial in the patient with lower back pain secondary to HNP[20,26] and in the patient with acute or chronic lower back pain and sciatica.[27,28] Systematic reviews of the literature have shown spinal manipulation is effective for the treatment of neck pain.[29] There have been no randomized controlled trials on the treatment of neck and arm pain with spinal manipulation, although case series have shown positive relief of neck pain and arm pain with spinal manipulation.[30-32] The combination of spinal manipulation and exercise has been shown in previous studies to be effective for chronic neck pain and lower back pain.[33-35]

The clinical rationale for medication-assisted spinal manipulation is that combined effects of the treatments will be more effective at addressing the multifactorial cause of spine and radicular pain syndromes than the use of component procedures alone. There have been 5 case series on the combination of ESI with anesthetics and various spinal manipulation techniques.[36] Although all of these studies reported positive results, there are distinct methodologic differences in terms of presenting pain syndromes, location of the injection, sample size, and manipulative techniques. As such, it is difficult to draw definitive conclusions with respect to effectiveness and safety of medication-assisted spinal manipulative techniques.

The purpose of this investigation was to determine if a combination of ESI with anesthetics and spinal manipulative therapy (SMT) offers promise as a relatively safe and efficacious nonsurgical treatment modality in patients with radicular pain syndromes. The thesis of this investigation is that the ESI with anesthetics addresses the inflammatory component of the pain syndrome,[17] whereas SMT may address the mechanical mechanism of pain[22] and, theoretically, the vascular mechanisms.[37] Both SMT and ESI with anesthetics theoretically address the central nervous system mechanisms of the radicular pain syndrome.[17,23,24] To evaluate this thesis, the current research describes the results of a retrospective case series in which radicular pain syndrome patients were treated with a simultaneous combination of ESI with anesthetics and SMT. The novelty of our data is that the current research is the largest known study, with a 12-month follow-up period. The current research is also the first to report on the use of medication-assisted spinal manipulative techniques in the cervical spine and to incorporate flexion distraction mobilization into the postinjection SMT.

Methods

Patients (n = 80) in this investigation were treated by the principal investigator (P.E.D.) between November 1996 and November 2000. The patients ranged in age from 21 to 76 years old with an average age of 43 ± 8.9 years. Forty-three percent of the patients were female patients and 57% were male patiens. We reviewed the charts of these patients retrospectively.

Inclusion criteria for patients were clinical signs of mechanical lower back pain, defined by ability to reproduce the pain syndrome with mechanical load on the spine. The patient also had signs and symptoms of radiculopathy, including loss of deep tendon reflex and myotomal paresis. For purposes of the present study, paresis was defined as 4/5 on the medical research council scale.[38] Additionally, all patients exhibited correlation of evidence of pathology, on MRI, to the spinal level of nerve root involvement. The patients also exhibited suboptimal improvement with a 4-week to 6-week clinical trial of flexion distraction mobilization; high-velocity, low-amplitude manipulation; stretching and stabilization exercises for the spine;[33-35] and nonsteroidal anti-inflammatory medications. Patients were excluded if they had symptoms and clinical findings compatible with cauda equina syndrome and if imaging studies showed evidence of root compression from causes other than HNP. Patients were also excluded if they were pregnant, had a known blood coagulation disorder, or had an allergy to local anesthetics.

Experimental Design

The patients in this retrospective analysis were treated with a combination of epidural injection and SMT, ie, spinal mobilization/manipulation techniques (see details below). Cervical and lumbar patients were subjected to the very same general protocol. The patients in this cohort were not subjected to any additional, nonroutine clinical procedures as part of the protocol. All patients were administered the epidural injection then immediately transferred in a non–weight-bearing position to the procedure room, where they were placed on the spinal manipulation treatment table. Spinal mobilization (low-velocity) consisting of flexion-distraction therapy was performed. Spinal manipulation (high-velocity, low-amplitude) was then performed, and the patient was monitored for a minimum of 30 minutes in the hospital and subsequently discharged from the hospital.

All patients subsequently underwent clinical analysis in the principal investigator's office 1 week postprocedure to determine the response to the procedure. The patient was released from active care if they exhibited significant improvement. If the patient reported either no improvement or temporary improvement with the procedure, then the principal investigator discussed with the patient the treatment option of receiving either a second procedure or in some cases a third procedure. Surgery was also presented as a treatment option if the patient reported no improvement. At 1 year after the last procedure involving epidural injection and SMT, the principal investigator performed a retrospective review of the clinical outcomes and any adverse effects that were reported as a result of the procedure. Thus, all the final results reported herein are based on a file review at 1 year after the last procedure.

Outcomes were based on improvement in clinical signs and symptoms, as well as the need for future surgical intervention. Outcomes were classified into 3 categories: significant improvement, temporary improvement, and no change. Significant improvement was defined as resolution of the pain syndrome, thus requiring no further nonoperative or surgical intervention.

Temporary improvement was delineated as a reduction of the pain syndrome; however, the need for further conservative care was warranted, but no surgical intervention was required. Patients who did not exhibit improvement were placed in the no change category, and all but 1 patient who refused surgery required subsequent surgical intervention. Adverse outcomes were based on record review, as well as review of hospital quality assurance documentation on the procedures performed.

Epidural Injection Procedures

The epidural injections were performed with the patient prone on the computed tomography (CT) or fluoroscopy table. The patient underwent preliminary imaging to determine the epidural injection site. The skin was anesthetized with 2% lidocaine solution. The neuroradiologist or anesthesiologist then advanced the 22-gauge spinal needle to the interlaminar or transforaminal space. Once the needle reached the epidural space, either contrast or air was injected to confirm the epidural location. Once entry into the epidural space was confirmed, the syringe was disconnected to assure the absence of a "wet tap." If no cerebrospinal fluid (CSF) was detected, the patient was then injected with a combination of lidocaine and Depo-Medrol. In the lumbar spine, the dosages were 80 mg of Depo-Medrol and 3 mL of 1% lidocaine, whereas in the cervical spine, the dosages were 40 mg of Depo-Medrol and 1 mL of 1% lidocaine.

Spinal Mobilization and Manipulation Procedures

All patients received the flexion-distraction mobilization procedure. Flexion-distraction tables allow for manually assisted mechanical traction to be applied to the spine along with passive ranges of motion. The basis of flexion-distraction manipulation is to open the posterior aspect of the functional spinal unit to allow greater sagittal diameter within the central and intervertebral canals.[30,37] This technique requires a specialized table with a joint mechanism in the middle that allows the clinician to manually move the patient through passive spinal flexion and extension. The patient was placed prone on the table and the clinician stood to the patient's side. In the lumbar spine, the clinician's cephalad hand stabilized the desired segment, applying countertraction forces, while the caudad hand moved the table through the desired range of motion.[39] In the cervical spine, the clinician's caudad hand stabilized the desired segment, applying a countertraction force, while the cephalad hand moved the table through the desired range of motion.[30]

The spinal manipulative procedures were high-velocity, low-amplitude thrusts, as commonly performed by practitioners of chiropractic and osteopathy.[40] The force applied to the spine in these procedures is reported to be delivered in approximately 200 ms, with linear vertebral displacements less than 10 mm.[40] The manual force, or thrusts, to the zygapophyseal joint are applied at the end of physiologic range of joint motion and extend into the so-called paraphysiologic zone of joint motion. The *paraphysiologic zone* is defined as the endpoint range of motion in which a joint can be passively forced without any deleterious effects.[40]

Table 1. *Symptoms and clinical diagnosis*

Cervical	Clinical finding	Lumbar	Clinical finding
C4-5 (2)	C5 Radiculopathy	L1-2 (1)	L2 Radiculopathy
C5-6 (11)	C6 Radiculopathy	L2-3 (1)	L2 Radiculopathy
C6-7 (7)	C7 Radiculopathy	L3-4 (4)	L4 Radiculopathy (2)
			L3 Radiculopathy (2)
		L4-5 (22)	L4 Radiculopathy (6)
			L5 Radiculopathy (16)
		L5-S1 (32)	L5 Radiculopathy (20)
			S1 Radiculopathy (12)

The values in parentheses refer to the number of cases.

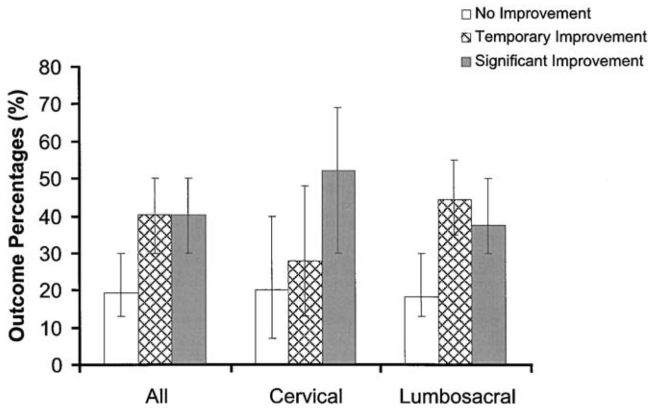

Fig 1. *Distribution of clinical outcomes for epidural injection procedures with spinal manipulation.* Error bars *denote the upper and lower limits of the 95% CIs for proportions.*

In the lumbar spine, the high-velocity, low-amplitude manipulative procedure was performed with the patient positioned into "side-posture." The clinician provided a manual contact on the tissues overlying the zygapophyseal joint of the involved lumbar segment. Using the right-handed Cartesian orthogonal coordinate system of movement as a reference, the primary force vector applied to the zygapophyseal joint was +θZ-axis translation (posterior-anterior) with a secondary vector consisting of +/− θY-axis rotation (right or left axial rotation). For cervical spinal manipulations, the patients were in a supine, semirecumbent position. The clinician applied a right hand contact to the paraspinal tissues overlying the involved cervical segment. The lateral aspect of digit 2 was applied to the tissues overlying the lamina-pedicle junction of the involved cervical segment. The primary force vector applied to the zygapophyseal joint was +θY (rotation), with a secondary vector consisting of +θZ rotation (lateral flexion).

Results

Symptomology and clinical diagnoses of the 80 patients are summarized in Table 1. Of the 80 patients, 67.5% (n = 54) underwent 1 epidural injection procedure with spinal manipulation. Twenty-five percent (n = 20) underwent 2 epidural injection procedures with spinal manipulation, whereas another 5 patients were treated 3 times. The decision to perform a second or third treatment procedure was based on the patient's clinical response to the previous treatment procedure and/or the patient's decision to continue with conservative care.

One patient, diagnosed with C6-7 HNP, underwent 4 epidural injection procedures with spinal manipulation to treat recurring pain symptoms. The treatment plan included 4 epidural injection procedures with spinal manipulation, since all but the second treatment procedure produced significant clinical improvements when documented at the clinical visit conducted 1 week after the procedure. In addition, the fourth treatment procedure was done approximately 1 year after the initial series of 3 treatment procedures. There were no complications during or after any of the 4 treatment procedures.

The majority of the patients showed a positive response with only 1 treatment procedure (76%). Surgery was deemed necessary in 13 patients after the first treatment procedure because of no clinical improvement. Of the 20 patients who underwent 2 treatment procedures, 4 patients showed no overall clinical response after the second treatment procedure, and surgical intervention was the next step in their clinical treatment course. All patients that underwent 3 treatment procedures did not require a surgical intervention.

Patients not showing any positive response to the epidural injection with SMT may indicate that the mass effect of the herniation was the predominant component of the radiculopathy. As such, the epidural injection with SMT would not be expected to positively affect this cause. Most of the patients later underwent a surgical intervention with good outcomes (n = 16). The other patient decided against a surgical intervention and continued with medical care at a chronic pain clinic with only transient relief of pain symptoms.

There were no complications associated with SMT. There were 3 complications associated with the epidural injection: 2 wet taps and 1 vagal response.

In summary, the frequency distribution of treatment procedures was 25 to the cervical spine and 88 to the lumbar spine. The majority of treatment procedures produced either temporary or significant clinical improvement (Fig 1). When summarizing outcomes by patient and lesion site, independent of the number of treatment procedures, 78.34% of the lumbar patients and 80% of the cervical patients had either temporary or significant clinical improvement.

Discussion

The results of the current study suggest that spinal manipulation procedures immediately postepidural injection offer a safe nonsurgical option for the patient with a radicular pain syndrome secondary to HNP. The data reported herein, however, do not address the question as to whether the combination of ESI with anesthetics and SMT offers a more positive clinical outcome than either component procedure alone. The current data can, however, be compared and contrasted with the body of literature that examines clinical outcomes for lumbar and cervical radiculopathy.

Traditionally, radicular pain syndromes secondary to HNP have been treated by surgical intervention, even though in-depth, prospective clinical outcome analyses are lacking. [41] There is also a paucity of literature comparing surgical interventions with conservative treatment options. In 1 report that used a 10-year follow-up, there were no significant differences in clinical outcomes of lumbar radicular pain syndromes between conservative care and surgical decompression.[42] Other comparisons between surgical versus conservative care for cervical radiculopathy showed statistical evidence for significant clinical improvement with conservative care during follow-up times of 4.6 months to 10.6 years.[43,44] Systematic reviews of the literature also indicate that conservative treatment of patients with radiculopathy may be effective.[20,45]

The current study corroborated the combination of 2 conservative management modalities for treating patients with radicular pain secondary to HNP. Theoretically, epidural injections (combination of steroid and anesthetic) are proposed to address the inflammatory and central components of spinal pain,[17] whereas spinal manipulation is proposed to address the mechanical and neural aspects of the pain syndrome.[22-24]

ESIs were first used to treat sciatica in the early 1950s. The rationale of using ESI for the treatment of spinal pain and radiculopathy include the anti-inflammatory action of the corticosteriod.[17] Methylprednisolone has a direct, reversible action on nociceptive axons that attenuate their activity level.[46] In addition, there is evidence that the local anesthetic may interrupt the sustained neural activity that produces and perpetuates pain and may also offer some degree of relaxation of the paraspinal muscle spasm.[17] Recent reviews evaluating the efficacy of ESI for back pain have shown that there is still insufficient evidence about the use of epidural steroids for back pain.[19,28] Nelemans et al[19] in their review opine that 1 of the reasons that the reports in the literature may be few and perhaps flawed is because of the complex and heterogeneous nature of low back pain.

Spinal manipulation continues to grow in acceptance in the spine care community. There are now at least 73 randomized controlled trials using spinal manipulation.[47] The most recent systematic review concluded that there was moderately strong evidence of the benefit with spinal manipulation for acute and chronic low back pain.[20] Burton et al[48] reported that manipulation was superior to chemonucleolysis for the treatment of symptomatic lumbar disk herniation. In 2 different studies, investigators reported that a statistically significant number of patients with lumbar and cervical disk herniation had good clinical outcome with treatment that included spinal manipulation and flexion-distraction mobilization procedures.[31,32] Cervical and lumbar radiculopathy have also been shown to be effectively treated with high-velocity, low-amplitude manipulation.[49,50] The physiologic effects of spinal manipulation include increased range of motion, changes in facet joint kinematics, increased pain tolerance, attenuation of alpha motor neuron excitability, and decrease in intradiskal pressure.[47]

Flexion-distraction mobilization procedures are performed on a specialized table. They create a combined long-axis distraction and flexion force on the lumbar spine and differ from traditional spinal manipulation by lack of a high-velocity, low-amplitude manual force.[37] Various theories abound as to the mechanical and physiologic effects of flexion-distraction procedures. Flexion has been shown to increase the size of the intervertebral foramen up to 31% in the cervical spine.[51] Both flexion and distraction have been shown to increase the central canal diameter in the cervical spine.[52] In the lumbar spine, flexion has also been reported to increase the central canal diameter, as well as the intervertebral canal diameter.[53] Traction has been shown to decrease intradiskal pressure and has been demonstrated by some investigators as being effective for treating low back pain.[54,55]

There are a limited number of studies evaluating the combination of ESI with anesthetics and SMT for treating symptoms of back pain.[56-60] Blomberg et al[58] reported on 48 acute or subacute low back pain patients who received intramuscular injections of steroids with anesthetics, as opposed to an epidural injection, followed by specific manual treatment involving manipulation and mobilization, muscle stretching, and autotraction. At 4 months follow-up, the patients who received the combination of intramuscular injection and manual therapy had superior outcomes compared with the 53 patients treated traditionally with rehabilitative exercises.[58] In a retrospective analysis of 10 chronic lower back pain patients, patients receiving a combination of ESI with anesthetics and SMT noted significant clinical improvements at 30 to 45 days follow-up, as opposed to patients who received ESI with anesthetics and SMT on separate occasions.[59] In another study, 500 patients who had not responded to conservative care for chronic lumbosciatic syndrome were treated with the combination of ESI with anesthetics and manual therapy.[60] The success rate of the combined therapy was 63%; success was defined as complete or near complete relief of all symptoms, lack of recurrence in the next 6 months, and no requirement for further treatment.[60] However, one third of their patients received general anesthesia, and manual therapy for all patients consisted of rotation of the spine and bilateral stretching of sciatic nerves as opposed to a short-lever, high-velocity, low-amplitude manipulation.[60] The other preliminary research in this area reported resolution of pain symptoms and improved function for 3 patients with low back pain and 2 patients with recalcitrant lumbar radiculopathy.[56,57]

Although the current research used similar empirical outcomes as the previous research reports, the data are representative of the greatest number of patients receiving a combination of ESI with anesthetics and SMT, and the follow-up period of 12 months is the longest. The overall success rate of 78% for treating cervical and lumbosacral radiculopathies with the combined therapy of ESI with anesthetics and SMT was greater than the previously reported success rate of 63% for treating chronic lumbosciatic syndrome with medication-assisted manual therapies.[60] The current research is also the first to report on the effectiveness of ESI with anesthetics and SMT for treating radicular pain syndromes of the cervical spine, ie, 80% of the cervical patients showed significant or temporary improvements. As such, our data results increase the literature base documenting the safety and theoretic efficacy of epidural injection with SMT for treating radicular pain syndromes of spinal origin.

The thesis supporting the use of a combination of ESI with anesthetics and SMT is to address the heterogeneous nature of spinal pain. By using a local infiltration of an anti-inflammatory agent and anesthetic, one may address the proposed inflammatory and centrally mediated causes of spinal pain.[17,19] SMT may address the neural and mechanical component of the syndrome.[47] The data reported cannot be extended to support this hypothesis. Previous studies using ESI have reported that 51.9%[61] and 25.8%[62] did not respond adequately enough to avoid future surgical intervention. In the present study, 22% of lumbar radiculopathy patients and 20% of cervical radiculopathy patients did not respond adequately to ESI with anesthetics and SMT, thus requiring surgical intervention. As previously opined by Nelemans et al[19] with respect to substantiating the efficacy of ESI for treating back pain, it is our supposition that future studies with a larger homogeneous group of patients may indicate promise in preventing surgical intervention with a combination of ESI with anesthetics and SMT.

Conclusion

Based on the rationale put forth, the use of spinal manipulation postepidural injection appears to be a safe nonoperative procedure for the treatment of the patient who has sustained either cervical or lumbar radiculopathy. The data also suggest that the combination of ESI with anesthetics and SMT may prove to be an efficacious nonoperative treatment modality in patients with radicular pain syndromes. We acknowledge, however, that there is a need for randomized controlled trials using a larger homogenous patient population to compare ESI with anesthetics and SMT to the component procedures alone.

References

1. Boden SD, McCowin PR, Davis DO, Dina TS, Mark AS, Wiesel S. Abnormal magnetic-resonance scans of the cervical spine in asymptomatic subjects. A prospective investigation. J Bone Joint Surg Am 1990;72:1178-84.
2. Borenstein DG, O'Mara JW, Boden SD, Lauerman WC, Jacobson A, Platenberg C, et al. The value of magnetic resonance imaging of the lumbar spine to predict low-back pain in asymptomatic subjects: a seven-year follow-up study. J Bone Joint Surg Am 2001;83:1306-11.
3. Matsumoto M, Fujimura Y, Suzuki N, Nishi Y, Nakamura M, Yabe Y, et al. MRI of cervical intervertebral discs in asymptomatic subjects. J Bone Joint Surg Br 1998;80:19-24.
4. Ito M, Incorvaia KM, Yu SF, Fredrickson BE, Yuan HA, Rosenbaum AE. Predictive signs of discogenic lumbar pain on magnetic resonance imaging with discography correlation. Spine 1998;23:1252-8.
5. Milette PC, Fontaine S, Lepanto L, Cardinal E, Breton G. Differentiating lumbar disc protrusions, disc bulges, and discs with normal contour but abnormal signal intensity. Magnetic resonance imaging with discographic correlations. Spine 1999; 24:44-53.
6. Rankine JJ, Gill KP, Hutchinson CE, Ross ER, Williamson JB. The clinical significance of the high-intensity zone on lumbar spine magnetic resonance imaging. Spine 1999;24: 1913-9.
7. Saifuddin A, Mitchell R, Taylor BA. Extradural inflammation associated with annular tears: demonstration with gadolinium-enhanced lumbar spine MRI. Eur Spine J 1999;8:34-9.
8. Gronblad M, Virri J, Ronkko S, Kiviranta I, Vanharanta H, Seitsalo S, et al. A controlled biochemical and immunohistochemical study of human synovial-type (group II) phospholipase A2 and inflammatory cells in macroscopically normal, degenerated, and herniated human lumbar disc tissues. Spine 1996;21:2531-8.
9. Hasue M. Pain and the nerve root. An interdisciplinary approach. Spine 1993;18:2053-8.
10. Lundborg G. Structure and function of the intraneural microvessals as related to trauma, edema, formation, and nerve function. Annual Meeting American Society of Surgery Hand March 8-11, 1975. Englewood, CO: American Society of Surgery of Hand.
11. Parke WW, Whalen JL. The vascular pattern of the human dorsal root ganglion and its probable bearing on a compartment syndrome. Spine 2002;27:347-52.
12. Saal JS. The role of inflammation in lumbar pain. Spine 1995; 20:1821-7.
13. Sugawara O, Atsuta Y, Iwahara T, Muramoto T, Watakabe M, Takemitsu Y. The effects of mechanical compression and hypoxia on nerve root and dorsal root ganglia. An analysis of ectopic firing using an in vitro model. Spine 1996;21:2089-94.
14. Winkelstein BA, Weinstein JN, DeLeo JA. The role of mechanical deformation in lumbar radiculopathy: an in vivo model. Spine 2002;27:27-33.
15. Ren K. Primary afferents and inflammatory hyperexcitability. Pain 1996;67:1-2.
16. Nakamura SI, Myers RR. Injury to dorsal root ganglia alters innervation of spinal cord dorsal horn lamina involved in nociception. Spine 2000;25:537-42.
17. Benzon HT. Epidural steroid injections for low back pain and lumbosacral radiculopathy. Pain 1986;24:277-95.
18. Di Rosa M, Calignano A, Carnuccio R, Ialenti A, Sautebin L. Multiple control of inflammation by glucocorticoids. Agents Actions 1986;17:284-9.
19. Nelemans PJ, deBie RA, deVet HC, Sturmans F. Injection

therapy for subacute and chronic benign low back pain. Spine 2001;26:501-15.
20. Vroomen PC, de Krom MC, Slofstra PD, Knottnerus JA. Conservative treatment of sciatica: a systematic review. J Spinal Disord 2000;13:463-9.
21. Johnson BA, Schellhas KP, Pollei SR. Epidurography and therapeutic epidural injections: technical considerations and experience with 5334 cases. AJNR Am J Neuroradiol 1999; 20:697-705.
22. Cramer GD, Tuck NR, Knudsen JT, Fonda SD, Schliesser JS, Fournier JT, et al. Effects of side-posture positioning and side-posture adjusting on the lumbar zygapophysial joints as evaluated by magnetic resonance imaging: a before and after study with randomization. J Manipulative Physiol Ther 2000; 23:380-94.
23. Dishman JD, Ball KA, Burke J. First prize: central motor excitability changes after spinal manipulation: a transcranial magnetic stimulation study. J Manipulative Physiol Ther 2002; 25:1-9.
24. Dishman JD, Bulbulian R. Spinal reflex attenuation associated with spinal manipulation. Spine 2000;24:2519-25.
25. Whittingham W, Nilsson N. Active range of motion in the cervical spine increases after spinal manipulation (toggle recoil). J Manipulative Physiol Ther 2001;24:552-5.
26. Shekelle PG, Adams AH, Chassin MR, Hurwitz EL, Brook RH. Spinal manipulation for low-back pain. Ann Intern Med 1992;117:590-8.
27. van Tulder MW, Koes BW, Bouter LM. Conservative treatment of acute and chronic nonspecific low back pain. A systematic review of randomized controlled trials of the most common interventions. Spine 1997;22:2128-56.
28. 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: 279-88.
29. Hurwitz EL, Aker PD, Adams AH, Meeker WC, Shekelle PG. Manipulation and mobilization of the cervical spine. A systematic review of the literature. Spine 1996;21:1746-59.
30. Kruse RA, Imbarlina F, De Bono VF. Treatment of cervical radiculopathy with flexion distraction. J Manipulative Physiol Ther 2001;24:206-9.
31. Beneliyahu DJ. Chiropractic management and manipulative therapy for MRI documented cervical disk herniation. J Manipulative Physiol Ther 1994;17:177-85.
32. Beneliyahu DJ. Magnetic resonance imaging and clinical follow-up: study of 27 patients receiving chiropractic care for cervical and lumbar disc herniations. J Manipulative Physiol Ther 1996;19:597-606.
33. Bronfort G, Goldsmith CH, Nelson CF, Boline PD, Anderson AV. Trunk exercise combined with spinal manipulative or NSAID therapy for chronic low back pain: a randomized, observer-blinded clinical trial. J Manipulative Physiol Ther 1996;19:570-82.
34. Bronfort G, Evans R, Nelson B, Aker PD, Goldsmith CH, Vernon H. A randomized clinical trial of exercise and spinal manipulation for patients with chronic neck pain. Spine 2001; 26:788-97.
35. Evans R, Bronfort G, Nelson B, Goldsmith CH. Two-year follow-up of a randomized clinical trial of spinal manipulation and two types of exercise for patients with chronic neck pain. Spine 2002;27:2383-9.
36. Kohlbeck FJ, Haldeman S. Medication-assisted spinal manipulation. Spine 2002;2:288-302.
37. Cox J. Low back pain: mechanism, diagnois and treatment. 6th ed. Baltimore: Williams & Wilkins; 1999. p. 261-72.
38. Principles of clinical myology: diagnosis and classification of muscle diseases–general considerations. In: Adams AH, Victor M, Ropper AH, editors. Principles of neurology. New York: McGraw-Hill; 1997. p. 1386-401.
39. Snow G. Chiropractic management of a patient with lumbar spinal stenosis. J Manipulative Physiol Ther 2001;24: 300-4.
40. Herzog W. The mechanical, neuromuscular, physiological effects produced by spinal manipulation. In: Herzog W, editor. Clinical biomechanics of spinal manipulation. New York: Churchill Livingstone; 2000. p. 191-207.
41. Winter RB. The prospective, randomized, controlled clinical trial in spine surgery: fact or fiction? Spine 1999;24:2550-2.
42. Weber H. Lumbar disc herniation. A controlled, prospective study with ten years of observation. Spine 1983;8: 131-140.
43. Heckmann JG, Lang CJ, Zobelein I, Laumer R, Druschky A, Neundorfer B. Herniated cervical intervertebral discs with radiculopathy: an outcome study of conservatively or surgically treated patients. J Spinal Disord 1999;12:396-401.
44. Sampath P, Bendebba M, Davis JD, Ducker T. Outcome in patients with cervical radiculopathy. Prospective, multicenter study with independent clinical review. Spine 1999; 24:591-7.
45. Samanta A, Beardsley J. Low back pain: which is the best way forward? BMJ 1999;318:1122-3.
46. Johansson A, Hao J, Sjolund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibres. Acta Anaesthesiol Scand 1990;34:335-8.
47. Meeker WC, Haldeman S. Chiropractic: a profession at the crossroads of mainstream and alternative medicine. Ann Intern Med 2002;136:216-27.
48. Burton AK, Tillotson KM, Cleary J. Single-blind randomised controlled trial of chemonucleolysis and manipulation in the treatment of symptomatic lumbar disc herniation. Eur Spine J 2000;9:202-7.
49. Cassidy JD, Thiel HW, Kirkaldy-Willis WH. Side posture manipulation for lumbar intervertebral disk herniation. J Manipulative Physiol Ther 1993;16:96-103.
50. Hubka MJ, Phelan SP, Delaney PM, Robertson VL. Rotary manipulation for cervical radiculopathy: observations on the importance of the direction of the thrust. J Manipulative Physiol Ther 1997;20:622-7.
51. Muhle C, Resnick D, Ahn JM, Sudmeyer M, Heller M. In vivo changes in the neuroforaminal size at flexion-extension and axial rotation of the cervical spine in healthy persons examined using kinematic magnetic resonance imaging. Spine 2001;26:E287-93.
52. Chen IH, Vasavada A, Panjabi MM. Kinematics of the cervical spine canal: changes with sagittal plane loads. J Spinal Disord 1994;7:93-101.
53. Inufusa A, An HS, Lim TH, Hasegawa T, Haughton VM, Nowicki BH. Anatomic changes of the spinal canal and intervertebral foramen associated with flexion-extension movement. Spine 1996;21:2412-20.
54. Gose EE, Naguszewski WK, Naguszewski RK. Vertebral axial decompression therapy for pain associated with herniated or degenerated discs or facet syndrome: an outcome study. Neurol Res 1998;20:186-90.
55. Ramos G, Martin W. Effects of vertebral axial decompression on intradiscal pressure. J Neurosurg 1994;81:350-3.
56. Aspegren DD, Wright RE, Hemler DE. Manipulation under epidural anesthesia with corticosteroid injection: two case reports. J Manipulative Physiol Ther 1997;20:618-21.
57. Ben-David B, Raboy M. Manipulation under anesthesia

combined with epidural steroid injection. J Manipulative Physiol Ther 1994;17:605-9.
58. Blomberg S, Hallin G, Grann K, Berg E, Sennerby U. Manual therapy with steroid injections–a new approach to treatment of low back pain A controlled multicenter trial with an evaluation by orthopedic surgeons. Spine 1994;19:569-577.
59. Nelson L, Aspegren D, Bova C. The use of epidural steroid injection and manipulation on patients with chronic low back pain. J Manipulative Physiol Ther 1997;20:263-6.
60. Warr AC, Wilkinson JA, Burn JM, Langdon L. Chronic lumbosciatic syndrome treated by epidural injection and manipulation. Practitioner 1972;209:53-9.
61. Snoek W, Weber H, Jorgensen B. Double blind evaluation of extradural methyl prednisolone for herniated lumbar discs. Acta Orthop Scand 1977;48:635-41.
62. Carette S, Leclaire R, Marcoux S, Morin F, Blaise GA, St-Pierre A, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. N Engl J Med 1997;336:1634-40.