

Retrospective Study

e Clinical Course of Cervical Percutaneous Epidural Neuroplasty in Single-Level Cervical Disc Disease with 12-Month Follow-up

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Background: Cervical disc disease is a common and occasionally disabling condition, occurring as a natural consequence of aging in the vast majority of the adult population. Percutaneous epidural neuroplasty (PEN) has been used to deliver highly concentrated drugs for chronic neck pain and to prevent scarring in cases refractory to conventional epidural blocks. However, the clinical course after PEN in cervical disc disease is not well-documented.

Objective: The purpose of this study was to evaluate the efficacy of cervical PEN for single-level cervical disc disease.

Study Design: A retrospective observational study.

Methods: A consecutive series of 100 patients who underwent cervical PEN for single-level disc disease (bulging or protrusion) were included in this study. Preoperatively, all patients underwent magnetic resonance imaging (MRI), and visual analog scale (VAS) scores as well as Odom's criteria were measured preoperatively and at post-operative follow-up visits (one, 3, 6, and 12 months).

Limitations: The results of this study are limited by the lack of a control group that did not undergo treatment with PEN.

Results: Additional block therapy was performed in 58 patients (58.0%). Subsequent surgery was performed in 10 patients (10.0%, excluded from data of clinical follow-up). Mean neck pain and VAS arm pain scores for all follow-up patients decreased from 6.82 and 4.74 preoperatively to 2.18 and 1.87 at 12 months after PEN ($P < 0.001$). More than 80% and 40% of all patients with and without additional block therapy after cervical PEN, respectively, showed good and excellent outcomes according to Odom's Criteria during 12 months of follow-up. During this follow-up period, no severe complications related to the procedure were observed.

Conclusion: Cervical PEN was shown to be a safe and effective treatment for neck and arm pain in single-level disc disease during 12 months of follow-up.

Key words: Neck pain, cervical disc disease, pain management, percutaneous epidural neuroplasty, adhesiolysis, clinical course

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Neck pain is usually caused by well-known etiologies such as cervical intervertebral disc, cervical facet joints, atlanto-axial and atlanto-occipital joints, ligaments, fascia, muscles, and

nerve root dura which are capable of transmitting pain (1-12). Cervical radicular pain can be caused by mechanical compression, nerve root irritation, and/or neurotoxicity (13). In addition, chronic edema

and fibrosis within a nerve root can alter its response threshold and increase sensitivity to pain (13). Cervical epidural steroid injections (ESI) have been used to treat radicular pain from herniated discs, spinal stenosis, chemical discs, chronic pain secondary to post-cervical surgery syndrome, and chronic neck pain of discogenic origin (14-19). However, the evidence for using cervical ESI has been a subject of debate. There is support for its application in cervical disc hernia tigon or radiculitis, as well as the management of axial or discogenic pain, spinal stenosis, and post-cervical surgery syndrome (14-17,20-34). Recently, cervical percutaneous epidural neuroplasty (PEN) was derived from lumbar PEN and has been used as a treatment option for cervical disc herniation (35-41). PEN is considered more effective than ESI, as it provides a more localized, selective block in the epidural space and is closer to the dorsal root ganglion and ventral aspect of the nerve root, possibly reducing the need for additional treatment (42). Previous reports have indicated that cervical PEN showed a favorable clinical effect in patients unresponsive to conventional ESI for cervical degenerative diseases (35,38,43). Another study reported that cervical PEN showed good clinical outcomes in the treatment of cervical disc herniation and could be considered a treatment modality for cervical disc herniation refractory to conservative treatment (38). However, the clinical course after PEN in cervical disc disease was not clearly investigated. Therefore, the aim of this study was to evaluate the efficacy of cervical PEN in patients with single-level cervical disc disease until 12 months follow-up with clinical course using Odom's Criteria.

METHODS

This retrospective observational study was approved by the Institutional Review Board (GTIRB-13-005), and written informed consent was obtained from all patients. Chronic posterior neck and radicular pain was diagnosed on the basis of clinical symptoms, neurological examination, and imaging studies including plain radiography and magnetic resonance imaging (MRI). Patients older than 20 years and younger than 80 years who had single-level herniated cervical disc, concordant with radicular pain demonstrated using MRI, were included in the study. Patients were included if they had pain lasting more than 3 months, which decreased by less than 50% at 4 weeks after conservative therapy and cervical pain procedures such as medial branch block and/or cervical ESI. Exclusion criteria were as follows: discordance between clinical symptoms and MRI find-

ings, clinical signs of spinal cord compression, symptoms of myelopathy, facet joint pain, instability, traumatic injuries, bleeding tendency, psychiatric disease, underlying systemic disease (except hypertension, diabetes, tuberculosis, and hepatitis), and medical history of prior spinal surgery.

Clinical Evaluation

All patients were asked to assess their disability using a visual analogue scale (VAS; 0–10) for neck pain (VAS neck) and arm pain (VAS arm), as well as Odom's Criteria (outcome rating as excellent, good, fair, or poor) (44) in order to evaluate the clinical effectiveness of PEN in terms of pain reduction and functional improvement. All patients were instructed to answer based on the average severity of their symptoms over the week before their visit. Successful pain relief was described as good or excellent using Odom's Criteria. The ratings were recorded before the procedure, and one, 3, 6, and 12 months after the procedure on an outpatient basis by an independent assessor.

Cervical Percutaneous Epidural Neuroplasty

Cervical PEN was performed similarly to previous reports (35,36,38,43). The patients were prepared and draped in a sterile manner in a prone position. After skin infiltration, an 18-gauge epidural needle (RX epidural needle, Coudé; Epimed International, Johnstown, NY) was inserted and advanced to the cervical epidural space using the loss of resistance technique at the level of C7-T1 interspace toward the midline under fluoroscopy. Once placement of the needle tip in the epidural space was confirmed, the tip was rotated cephalad. Epidurography was performed to confirm needle position in the epidural space. A Racz epidural catheter (VERSA-KATH®, Epimed International, Inc.) was placed directly into the herniated disc level under fluoroscopic control, and 0.5–1 mL of contrast media (IOBRIX®, ACCUZEN, Seoul, Korea) was injected to check warning contrast filling into the intravascular, subarachnoid, or perivenous counter spaces. For the best outcome, the optimal catheter position was considered to be the junction between cervical disc pathology and the ventral side of the dorsal nerve roots (Fig. 1) (45). After confirming the proper position of the catheter tip, 1,500 units of hyaluronidase (HYALOSE®, IKSU Pharmacy Co., Gyeonggi-do, Korea) suspended in 2 mL of preservative-free normal saline and a 5 mL mixture of 0.2% bupivacaine and 5 mg of triamcinolone was injected. After all procedures were completed, a modified one-day procedure proto-

col by Manchikanti et al (46,47) was applied. Patients were asked to perform neural flossing exercises to break up weakened scar tissue and to prevent further scar tissue development (40).

Statistical Analysis

Student's t-tests and chi-square tests were conducted to estimate the clinical outcomes after cervical PEN. All statistical analyses were performed using SPSS software (SPSS Inc., Chicago, IL, USA), and statistical significance was defined as $P < 0.05$.

RESULTS

In total, 100 patients (53 men and 47 women) completed the 12-month follow-up, and the mean age was 48.8 ± 9.1 years old with a range of 29 to 68 years. The mean duration of pre-procedural pain was 26.6 ± 50.6 months with a range of 4 to 360 weeks. The mean duration between cervical ESI and cervical PEN was 11.2 ± 4.7 weeks, and the mean duration between cervical medial branch block and cervical PEN was 4.7 ± 2.3 weeks. The most frequently involved cervical level was C5/6 (46 patients) followed by C6/7 (27 patients), C4/5 (19 patients), and C3/4 (8 patients) (Table 1). Protruding discs were present in 82 patients (82.0%) and 18 patients (18.0%) had bulging discs.

Additional block therapy was performed in 58 patients (58.0%), with use of medial branch block in 37 patients, cervical ESI in 5 patients, and both of these in 16 patients. The main cause of additional block therapies was remnant central neck pain aggravated by cervical facet movement and/or remnant cervical root irritation pain until 6 weeks after cervical PEN. Of the 100 patients, 10 patients (10.0%) with a poor outcome elected subsequent surgery during the follow-up period. The clinical results of patients who underwent subsequent surgery were excluded from the clinical analysis. Mean neck pain and arm pain VAS scores for all follow-up patients (except the 10 patients who underwent subsequent surgery) decreased, respectively, from 6.82 ± 1.65 and 4.74 ± 2.19 preoperatively to 1.48 ± 2.72 and 1.37 ± 2.13 at one month, 2.11 ± 2.75 and 1.80 ± 2.32 at 3 months, 2.26 ± 2.56 and 1.71 ± 1.95 at 6 months, and 2.18 ± 2.40 and 1.87 ± 2.22 at 12 months (Fig. 2 and Fig. 3). Clinically significant differences were observed for all follow-up time points when compared to preoperative scores ($P < 0.001$) and post-operative one month ($P < 0.05$) scores for VAS neck pain, and at all follow-up periods compared to preoperative ($P < 0.001$) and post-operative 3 months compared to post-operative one



Fig. 1. Cervical percutaneous epidural neuroplasty (arrow indicates the catheter location).

Table 1. Demographic data of all the patients.

Number	100
Male Ratio	53 (53.0%)
Mean Age	48.8 ± 9.1
Duration (month)	26.6 ± 50.6
Level	
C3/4	8 (8.0%)
C4/5	19 (19.0%)
C5/6	46 (46.0%)
C6/7	27 (27.0%)
Disc Type	
Bulging	18 (18.0%)
Protrusion	82 (82.0%)
HTN	21 (21.0%)
DM	28 (28.0%)
Tuberculosis	3 (3.0%)
Hepatitis	4 (4.4%)

month ($P = 0.025$) for VAS neck pain. No statistical differences were observed when comparing VAS neck and arm pain at post-operative 6 months.

Patient satisfaction at 12 months post-procedure was measured using Odom's Criteria, excluding patients who underwent subsequent surgery (Fig. 4). Odom's Criteria at post-operative one month ranked

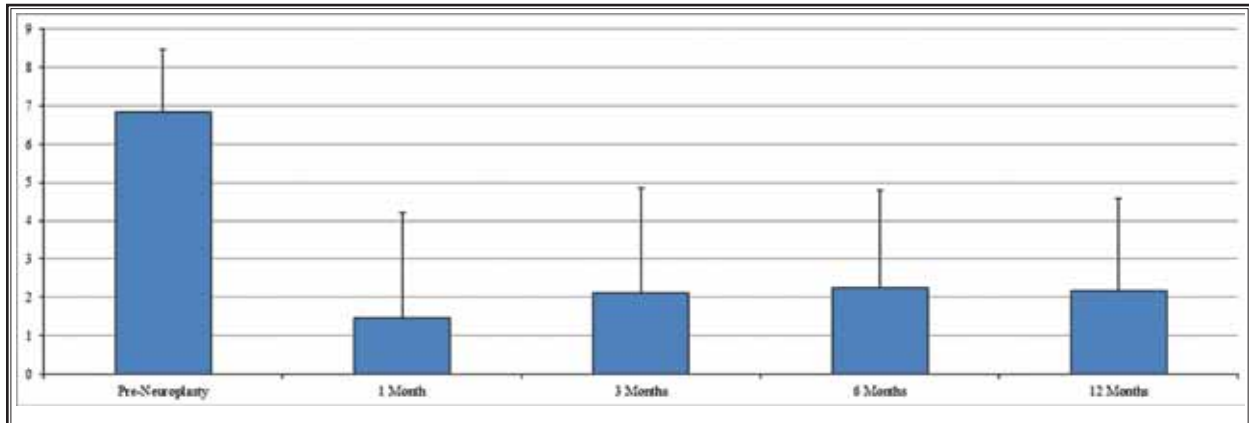


Fig. 2. Total mean VAS scores for neck pain after percutaneous epidural neuroplasty were significantly lower than preoperative scores. (All follow-up VAS scores had a statistical difference of less than 0.001 when compared to pre-neuroplasty VAS scores.)

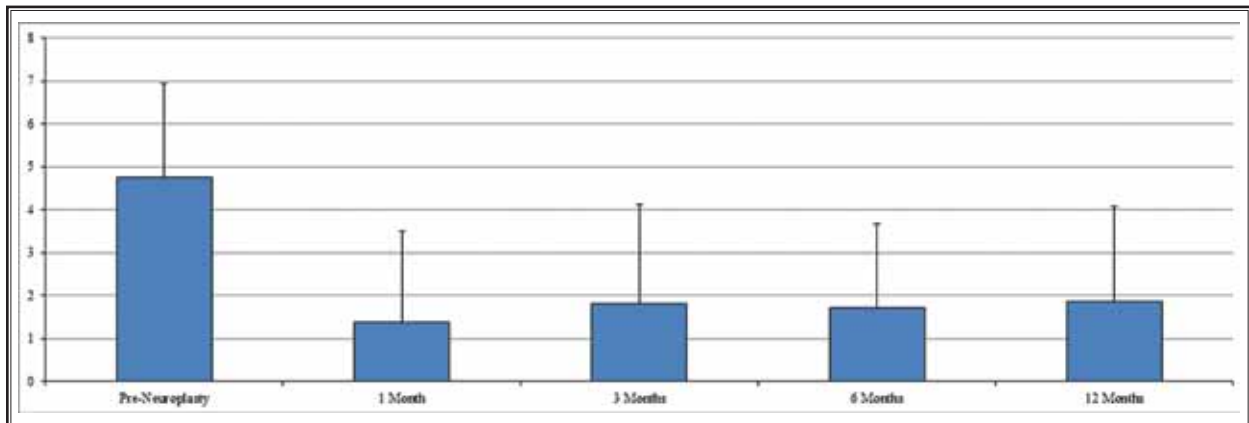


Fig. 3. Total mean VAS scores for arm pain after percutaneous epidural neuroplasty were significantly lower than preoperative scores. (All follow-up VAS scores have a statistical difference of less than 0.001 when compared to pre-neuroplasty VAS scores.)

63 patients (70.0%) as excellent, 16 patients (17.8%) as good, and 11 patients (12.2%) as fair. By 3 months follow-up, 12 patients changed from excellent to good, 5 patients from excellent to fair, 9 patients from good to excellent, 4 patients from good to fair, 5 patients from fair to good, and one patient from fair to poor. Therefore, at post-operative 3 months, outcomes were ranked as excellent in 55 patients (61.1%), good in 20 patients (22.2%), fair in 14 patients (15.6%), and fair in one patient (1.1%). By 6 months follow-up, 6 patients changed from excellent to good, 4 patients from excellent to fair, one patient from excellent to poor, 7 patients from good to excellent, 5 patients from good to fair, 11 patients from fair to good, one patient from fair to poor, and one patient from poor to good. Therefore, at post-operative 6 months, outcomes were

ranked as excellent in 51 patients (56.7%), good in 26 patients (28.8%), fair in 11 patients (12.2%), and fair in 2 patients (2.2%). Finally, by 12 months follow-up, 8 patients changed from excellent to good, 2 patients from excellent to fair, 3 patients from excellent to poor, 7 patients from good to excellent, 4 patients from good to fair, 2 patients from fair to excellent, 7 patient from fair to good, and one patient from poor to good. At the final assessment using Odom's Criteria at post-operative 12 months, outcomes were excellent in 47 patients (52.2%), good in 31 patients (34.5%), fair in 8 patients (8.9%), and fair in 4 patients (4.4%). Including patients with subsequent surgery, the final distribution of positive outcomes according to Odom's Criteria (excellent and good) were observed in 78 patients (86.7% among 90 patients and 78.0% among 100 patients).

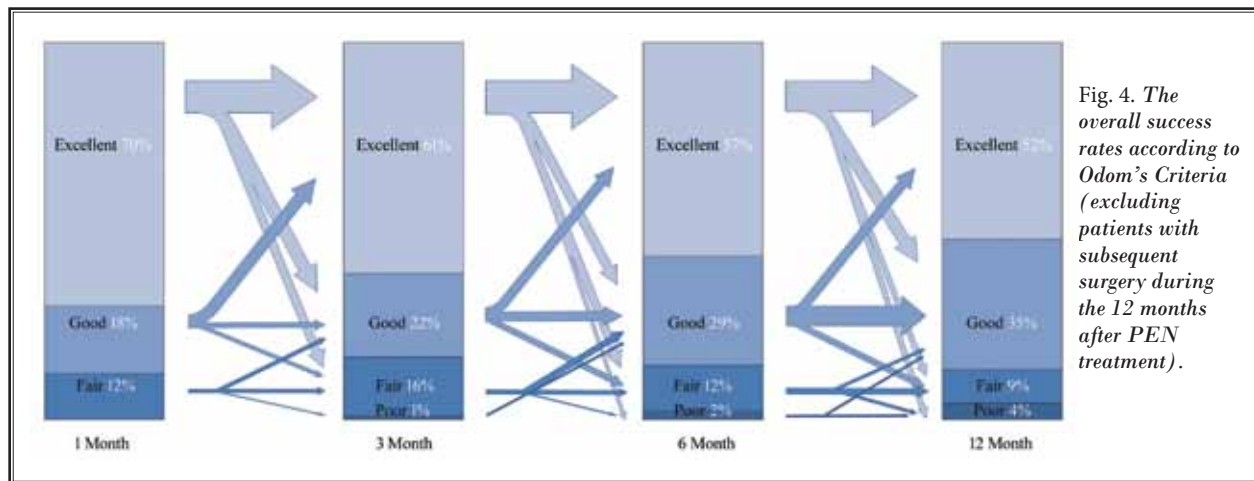


Fig. 4. The overall success rates according to Odom's Criteria (excluding patients with subsequent surgery during the 12 months after PEN treatment).

Additionally, cervical PEN provided excellent outcomes in 42.0% of patients (of 100) without additional block therapy. Patients with excellent outcomes received additional block therapy during the 12 month follow-up period (83.0%, 39 among 47 patients), including medial branch block (34 patients), cervical ESI (one patient), and both types of block (4 patients). No serious complications occurred in this series during the 12 month follow-up period.

Discussion

Local anesthetic mixed with corticosteroid may have additional benefits beyond the direct anesthetic effects. Lidocaine has been shown to have an anti-inflammatory effect on nucleus pulposus-induced nerve injury (48,49). The rationale for corticosteroid instillation also includes an anti-inflammatory effect. Cervical herniated disk specimens have demonstrated increased levels of phospholipase A2, which plays a role in inflammation of the nerve root and may be neurotoxic. However, epidural steroids have been shown to inhibit phospholipase A2 activity and reduce symptoms (50-53). With increased delivery of these substances to the localized epidural space (closer to the dorsal root ganglion and ventral aspect of the nerve root), cervical PEN showed good clinical results compared to ESI (45). The indication for cervical PEN is broad, including cervicgia or cervical radiculopathy with any of the following origins: failed neck surgery syndrome, cervical disc bulge with or without cervical radiculopathy, cervical radiculopathy, epidural fibrosis, and spinal stenosis (36). Further, clinical studies examining cervical PEN are sparse. In the literature, 4 reports indicated that cervical PEN had favorable clinical effects for patients with

cervical disc herniation and/or central stenosis who did not respond to fluoroscopically guided epidural injections (35,38,43,45).

A prospective study by Park et al (43) detailed the performance of cervical PEN in 39 patients with central cervical stenosis. All patients had a reinforced navigable catheter inserted at T1-2 advanced cephalad and then received an initial solution which contained local anesthetic, hyaluronidase, and corticosteroid. The follow-up periods were at 2 weeks and 6 months, and the outcome measure was a Roland 5-point patient satisfaction scale (0 indicated no pain and 5 indicated unbearable pain). Three patients (7.7%) elected to have spinal surgery during the follow-up period. Pain improvement was demonstrated in 30 of 39 patients (77.0%) at 2 weeks and in 28 of 39 patients (71.8 %) at 6 months. However, this exploratory study did not report baseline data, so it is difficult to interpret the follow-up data (39).

A retrospective study by Park et al (35) evaluated the outcome of cervical PEN in 128 patients with cervical disc herniation. Patients with refractory radicular pain were included in the study, but patients with a prior history of surgery were excluded. Radiopaque epidural catheters were placed at C7-T1 or T1-T2 in all patients, and advanced cephalad to the level of disc herniation. Adhesiolysis using hyaluronidase solution was performed, followed by delivery of ropivacaine with dexamethasone. Follow-up was performed at one day, and one, 3, 6, and 12 months post-treatment. Twelve patients received cervical ESI one month after adhesiolysis due to remnant pain. Five patients (3.9%) elected to have spinal surgery during the follow-up period. Overall, the numeric rating scale results showed significant improvement at all time points for arm (from

73.0 at baseline to 8.3 at 12 months) and neck pain (from 77.0 at baseline to 4.1 at 12 months). Mean neck disability scores also decreased from a baseline of 17.5 to 2.3 at 12 months follow-up. No serious complications were reported. Although the evidence is weak, this study suggests that some patients with spinal stenosis and disc herniation who failed conservative therapy might benefit from cervical PEN.

An observational study by Moon et al (38) evaluated the clinical outcomes of cervical PEN in 169 patients with posterior neck and upper extremity pain and the predictive factors for unsuccessful cervical PEN results. An epidural catheter was placed at T1-T2, and then advanced and maneuvered into the target disc herniation lesion. Hyaluronidase in preservative-free normal saline was injected via epidural catheter, and subsequently a mixture of bupivacaine and triamcinolone was injected. Follow-up visits were performed through 12 months post-treatment. Three patients (1.8%) elected to have spinal surgery during the follow-up period. Successful outcomes (50% or greater reduction on total pain rating scale compared to the pre-procedure value, and at least a 40% reduction on the neck pain and disability scale) were observed in 108 patients (63.9%) at one month following the procedure, in 109 patients (64.5%) at 3 months, in 96 patients (56.8%) at 6 months, and in 89 patients (52.7%) at 12 months. Previous surgery, spondylolisthesis, and ossification of the posterior longitudinal ligament were significantly associated with unsuccessful outcomes ($P < 0.05$). There were no adverse events except for transient local pain associated with the procedure. Although the lack of a placebo group was one of the limitations, this study suggested that cervical PEN may be an effective treatment for pain reduction and functional improvement in patients with cervical spinal pain who did not respond to conservative treatment, possibly decreasing surgical demand.

A randomized control study by Ji et al (45) compared the clinical efficacy of cervical PEN and cervical ESI. Eighty patients with neck pain from single-level cervical disease with and without radiculopathy were included. Patients were randomly assigned into 2 groups: cervical PEN or ESI. Both the cervical PEN and ESI groups showed a better neck disability index (NDI) recovery and a greater reduction in VAS score at post-operative 6 months ($P < 0.001$). The cervical PEN group demonstrated a better NDI score at post-operative 6 months than the ESI group ($P = 0.014$), while there were no differences at 2, 4, and 12 months. The cervical PEN

group showed lower VAS scores at all follow-up time points compared to the ESI group ($P < 0.050$). Symptom relief was sustained for a significantly longer duration in the cervical PEN group than in the ESI group (23.4 vs. 20.5 weeks, $P < 0.001$). Therefore, the investigators concluded that cervical PEN was superior to ESI in terms of better NDI recovery (at 6 months) and greater reduction in VAS score (until 12 months) for treating single-level cervical disc herniation. They also reported that better outcomes with cervical PEN may have been achieved via a more localized, selective block in the epidural space closer to the dorsal root ganglion and ventral aspect of the nerve root.

Similar to 4 previous studies (35,38,43,45), this study evaluated the clinical course and effectiveness of cervical PEN in single-level cervical disc disease. A total of 100 patients with single-level herniated cervical disc with concordant radicular pain demonstrated by MRI were included in the study. A Racz catheter was advanced through C7-T1, and the catheter tip was placed in the target disc herniation lesion. Hyaluronidase with preservative-free normal saline and a mixture of bupivacaine and triamcinolone were subsequently injected. The hyaluronidase (HYALOSE®) used in this study was a powder, so additional volume was not added to cocktails. Follow-up visits were performed at one, 3, 6, and 12 months after cervical PEN. Fifty-eight patients received additional block therapy during the follow-up period after adhesiolysis due to remnant pain. Compared to previous studies, a relatively high proportion of patients ($n = 10$, 10.0% vs. 1.8~7.7%) elected to have spinal surgery within one month after the operation. There were significant decreases in mean VAS for neck pain (from 6.82 at preoperative to 2.18 at 12 months) and arm pain scores (from 4.74 to 1.87 at 12 months) at all follow-up time points. Indeed, during 12 months, more than 80% of all patients who underwent PEN showed good and excellent outcomes according to Odom's Criteria. Clinical results in recent studies showed better outcomes compared to the previous 3 studies, although different clinical methods were applied. We propose that these favorable results might be derived from the additional block treatments (medial branch block and/or cervical ESI) which were performed in 58 patients (58.0%) during follow-up. The additional treatment may have also interfered with the clinical course after cervical PEN: the outcome of 50 patients increased according to Odom's Criteria, such as good to excellent and fair to good. There were no severe complications related to the procedure. This study suggests

that cervical PEN is a safe and effective treatment for neck and arm pain in single-level disc disease, similar to the results of 4 previous studies (35,38,43,45).

The PEN procedure is considered to be more effective than ESI as it comprises a more localized, selective block in the epidural space placed closer to the dorsal root ganglion and ventral aspect of the nerve root, between the nerve and the disc herniated particle where micro-adhesion by the inflamed nerve is suspected (45). If micro adhesion by discal irritation with an inflamed nerve is present, this micro-adhesion could be removed by mechanical adhesiolysis (catheter indwelling), chemical adhesiolysis (hyaluronidase), and hydrostatic adhesiolysis (radio-opaque dye and saline) as the authors previously reported (45). The more favorable results for cervical PEN are believed to be a result of a more localized, selective block in the epidural space placed closer to the dorsal root ganglion and ventral aspect of the nerve root compared to ESI. By greater selective targeting of lesions, symptom relief was maintained for a longer duration using the cervical PEN treatment.

There were several limitations to this study. First, there was no control group. Secondly, this study included patients with single-level disc disease and data were categorized according to a simple classifier (bulg-

ing and protrusion). In spite of these limitations, we reported the efficacy of cervical PEN among single-level cervical disc disease patients. This study suggests that cervical PEN can be used as another treatment strategy for patients with cervical disc disease. Large-scale, randomized controlled studies with longer follow-up durations are required to examine the effects of cervical PEN in patients with cervical disc degeneration.

CONCLUSION

This study evaluated the clinical course of cervical PEN and showed that the procedure is a safe and effective treatment for single-level disc disease up to 12 months of follow-up. Cervical PEN should be considered as a next-step treatment modality for treating single-level disc disease refractory to conservative treatment.

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REFERENCES

1. Benyamin RM, Singh V, Parr AT, Conn A, Diwan S, Abdi S. Systematic review of the effectiveness of cervical epidurals in the management of chronic neck pain. *Pain Physician* 2009; 12:137-157.
2. Bogduk N. Pathology. In: *Medical management of acute cervical radicular pain: An evidence based approach*. Newcastle, Newcastle Bone and Joint Institute, Royal Newcastle Hospital. 1999. pp. 13-18
3. McCarron RF, Wimpee MW, Hudkins PG, Laros GS. The inflammatory effects of nucleus pulposus: A possible element in the pathogenesis of low back pain. *Spine (Phila Pa 1976)* 1987; 12:760-764.
4. Olmarker K, Blomquist J, Strömberg J, Nannmark U, Thomsen P, Rydevik B. Inflammation properties of nucleus pulposus. *Spine (Phila Pa 1976)* 1995; 20:665-669.
5. Olmarker K, Nordborg C, Larsson K, Rydevik B. Ultrastructural changes in spinal nerve roots induced by autologous nucleus pulposus. *Spine (Phila Pa 1976)* 1996; 27:411-414.
6. Kawakami M, Tamaki T, Hashizume H, Weinstein JN, Meller ST. The role of phospholipase A2 and nitric oxide in pain-related behavior produced by an allograft of intervertebral disc material to the sciatic nerve of the rat. *Spine (Phila Pa 1976)* 1997; 22:1074-1079.
7. Kang JD, Georgescu HI, McIntyre-Larkin L, Stefanovic-Racic M, Evans CH. Herniated cervical intervertebral discs spontaneously produce matrix metalloproteinases, nitric oxide, interleukin-6, and prostaglandin E2. *Spine (Phila Pa 1976)* 1995; 20:2373-2378.
8. Kang JD, Bohlman HH. Current concepts review: Evaluation and treatment of cervical spondylotic myelography. *Pittsburgh Ortho J* 1994; 5:14-25.
9. 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 (Phila Pa 1976)* 1998; 23:2517-2523.
10. Genevay S, Finckh A, Payer M, Mezin F, Tessitore E, Gabay C, Guerne PA. Elevated levels of tumor necrosis factor-alpha in periradicular fat tissue in patients with radiculopathy from herniated disc. *Spine (Phila Pa 1976)* 2008; 33:2041-2046.
11. Sugiura A, Ohtori S, Yamashita M, Inoue G, Yamauchi K, Koshi T, Suzuki M, Norimoto M, Orita S, Eguchi Y, Takahashi Y, Watanabe TS, Ochiai N, Takaso M, Takahashi K. Existence of nerve growth factor receptors, tyrosine kinase a and p75 neurotrophin receptors in intervertebral discs and on dorsal root ganglion neurons innervating intervertebral discs in rats. *Spine (Phila Pa 1976)* 2008; 33:2047-2051.
12. Yamashita M, Ohtori S, Koshi T, Inoue G, Yamauchi K, Suzuki M, Takahashi K. Tumor necrosis factor-alpha in the nucleus pulposus mediates radicular pain, but not increase of inflammatory peptide, associated with nerve damage in mice. *Spine (Phila Pa 1976)* 2008; 33:1836-1842.
13. Rao R. Neck pain, cervical radiculopathy, and cervical myelopathy: Pathophysiology, natural history, and clinical evaluation. *J Bone Joint Surg Am* 2002; 84-A: 1872-1881.

14. Boswell MV, Trescot AM, Datta S, Schultz DM, Hansen HC, Abdi S, Sehgal N, Shah RV, Singh V, Benyamin RM, Patel VB, Buenaventura RM, Colson JD, Corderner HJ, Epter RS, Jasper JF, Dunbar EE, Atluri SL, Bowman RC, Deer TR, Swicegood JR, Staats PS, Smith HS, Burton AW, Kloth DS, Giordano J, Manchikanti L. Interventional techniques: Evidence based practice guidelines in the management of chronic spinal pain. *Pain Physician* 2007; 10:7-111.
15. Peloso PMJ, Gross A, Haines T, Trinh K, Goldsmith CH, Burnie SJ; Cervical Overview Group. Medicinal and injection therapies for mechanical neck disorders. *Cochrane Database Syst Rev* 2007; 3:CD000319.
16. Abdi S, Datta S, Trescot AM, Schultz DM, Adlaka R, Atluri SL, Smith HS, Manchikanti L. Epidural steroids in the management of chronic spinal pain: A systematic review. *Pain Physician* 2007; 10:185-212.
17. Manchikanti L, Singh V, Derby R, Schultz DM, Benyamin RM, Prager JP, Hirsch JA. Reassessment of evidence synthesis of occupational medicine practice guidelines for interventional pain management. *Pain Physician* 2008; 11:393-482.
18. Diwan S, Manchikanti L, Benyamin RM, Bryce DA, Geffert S, Hameed H, Sharma ML, Abdi S, Falco FJ. Effectiveness of cervical epidural injections in the management of chronic neck and upper extremity pain. *Pain Physician* 2012; 15:E405-E434.
19. Huston CW. Cervical epidural steroid injections in the management of cervical radiculitis: Interlaminar versus transforaminal. A review. *Curr Rev Musculoskelet Med* 2009; 2:30-42.
20. Manchikanti L, Falco FJ, Singh V, Benyamin RM, Racz GB, Helm S, II, Caraway DL, Calodney AK, Snook LT, Smith HS, Gupta S, Ward SP, Grider JS, Hirsch JA. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part I: Introduction and general considerations. *Pain Physician* 2013; 16:S1-S48.
21. Manchikanti L, Abdi S, Atluri S, Benyamin RM, Boswell MV, Buenaventura RM, Bryce DA, Burks TA, Caraway DL, Calodney AK, Cash KA, Christo PJ, Cohen SP, Colson J, Conn A, Corderner HJ, Coubarous S, Datta S, Deer TR, Diwan S, Falco FJ, Fellows B, Geffert S, Grider JS, Gupta S, Hameed H, Hameed M, Hansen H, Helm S 2nd, Janata JW, Justiz R, Kaye AD, Lee M, Manchikanti KN, McManus CD, Onyewu O, Parr AT, Patel VB, Racz GB, Sehgal N, Sharma ML, Simopoulos TT, Singh V, Smith HS, Snook LT, Swicegood JR, Vallejo R, Ward SP, Wargo BW, Zhu J, Hirsch JA. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: Guidance and recommendations. *Pain Physician* 2013; 16:S49-S283.
22. Kaye AD, Manchikanti L, Abdi S, Atluri S, Bakshi S, Benyamin R, Boswell MV, Buenaventura R, Candido KD, Corderner HJ, Datta S, Doulatram G, Gharibo CG, Grami V, Gupta S, Jha S, Kaplan ED, Malla Y, Mann DP, Nampiarampil DE, Racz G, Raj P, Rana MV, Sharma ML, Singh V, Soin A, Staats PS, Vallejo R, Wargo BW, Hirsch JA. Efficacy of epidural injections in managing chronic spinal pain: A best evidence synthesis. *Pain Physician* 2015; 18:E939-E1004.
23. Helm S, II, Racz GB, Gerdemeseyer L, Justiz R, Hayek SM, Kaplan ED, El Terany MA, Knezevic NN. Percutaneous and endoscopic adhesiolysis in managing low back and lower extremity pain: A systematic review and meta-analysis. *Pain Physician* 2016; 19:E245-E282.
24. Manchikanti L, Nampiarampil DE, Candido KD, Bakshi S, Grider JS, Falco FJ, Sehgal N, Hirsch JA. Do cervical epidural injections provide long-term relief in neck and upper extremity pain? A systematic review. *Pain Physician* 2015; 18:39-60.
25. Manchikanti L, Malla Y, Cash KA, McManus CD, Pampati V. Fluoroscopic cervical interlaminar epidural injections in managing chronic pain of cervical post-surgery syndrome: Preliminary results of a randomized, double-blind active control trial. *Pain Physician* 2012; 15:13-26.
26. Manchikanti L, Cash KA, Pampati V, Malla Y. Two-year follow-up results of fluoroscopic cervical epidural injections in chronic axial or discogenic neck pain: A randomized, double-blind, controlled trial. *Int J Med Sci* 2014; 11:309-320.
27. Manchikanti L, Malla Y, Cash KA, McManus CD, Pampati V. Fluoroscopic epidural injections in cervical spinal stenosis: Preliminary results of a randomized, double-blind, active control trial. *Pain Physician* 2012; 15:E59-E70.
28. Manchikanti L, Cash KA, Pampati V, Wargo BW, Malla Y. Management of chronic pain of cervical disc herniation and radiculitis with fluoroscopic cervical interlaminar epidural injections. *Int J Med Sci* 2012; 9:424-434.
29. Manchikanti L, Nampiarampil DE, Manchikanti KN, Falco FJ, Singh V, Benyamin RM, Kaye AD, Sehgal N, Soin A, Simopoulos TT, Bakshi S, Gharibo CG, Gilligan CJ, Hirsch JA. Comparison of the efficacy of saline, local anesthetics, and steroids in epidural and facet joint injections for the management of spinal pain: A systematic review of randomized controlled trials. *Surg Neurol Int* 2015; 6:S194-S235.
30. Manchikanti L, Rivera JJ, Pampati V, Damron KS, McManus CD, Brandon DE, Wilson SR. One day lumbar epidural adhesiolysis and hypertonic saline neurolysis in treatment of chronic low back pain: A randomized, double-blind trial. *Pain Physician* 2004; 7:177-186.
31. Manchikanti L, Manchikanti KN, Gharibo CG, Kaye AD. Efficacy of percutaneous adhesiolysis in the treatment of lumbar post surgery syndrome. *Anesth Pain Med* 2016; 6:e26172.
32. Manchikanti L, Cash KA, McManus CD, Pampati V. Assessment of effectiveness of percutaneous adhesiolysis in managing chronic low back pain secondary to lumbar central spinal canal stenosis. *Int J Med Sci* 2013; 10:50-59.
33. Manchikanti L, Singh V, Cash KA, Pampati V. Assessment of effectiveness of percutaneous adhesiolysis and caudal epidural injections in managing lumbar post surgery syndrome: A 2-year follow-up of randomized, controlled trial. *J Pain Res* 2012; 5:597-608.
34. Manchikanti L, Knezevic NN, Boswell MV, Kaye AD, Hirsch JA. Epidural injections for lumbar radiculopathy and spinal stenosis: A comparative systematic review and meta-analysis. *Pain Physician* 2016; E365-E410.
35. Park EJ, Park SY, Lee SJ, Kim NS, Koh DY. Clinical outcomes of epidural neuroplasty for cervical disc herniation. *J Korean Med Sci* 2013; 28:461-465.
36. Viesca CO, Racz GB, Day MR. Special techniques in pain management: Lysis of adhesions. *Anesthesiol Clin North America* 2003; 21:745-766.
37. Talu GK, Erdine S. Complications of epidural neuroplasty: A retrospective evaluation. *Neuromodulation* 2003; 6:237-247.
38. Moon DE, Park HJ, Kim YH. Assessment of clinical outcomes of cervical epidural neuroplasty using a Racz-catheter and

- predictive factors of efficacy in patients with cervical spinal pain. *Pain Physician* 2015; 18:E163-E170.
39. Lee F, Jamison DE, Hurley RW, Cohen SP. Epidural lysis of adhesions. *Korean J Pain* 2014; 27:3-15.
 40. Racz GB, Heavner JE, Smith JP, Noe CE, Al-Kaisy A, Matsumoto T, Lee SC, Nagy L. Epidural lysis of adhesions and percutaneous neuroplasty. In: Racz GB, Noe CE (eds.) *Pain and Treatment*, InTech Rijeka, 2014; 337-371.
 41. Racz GB, Heavner JE. Complications associated with lysis of epidural adhesions and epiduroscopy. In: Neal JM, Rathmell JP (eds). *Complications in Regional Anesthesia & Pain Medicine*. Saunders Elsevier, Philadelphia, PA, 2007. pp 301-311.
 42. Heavner JE, Racz GB, Raj P. Percutaneous epidural neuroplasty: Prospective evaluation of 0.9% NaCl versus 10% NaCl with or without hyaluronidase. *Reg Anesth Pain Med* 1999; 24:202-207.
 43. Park CH, Lee SH, Lee SC. Preliminary results of the clinical effectiveness of percutaneous adhesiolysis using a Racz catheter in the management of chronic pain due to cervical central stenosis. *Pain Physician* 2013; 16:353-358.
 44. Odom GL, Finney W, Woodhall B. Cervical disc lesions. *JAMA* 1958; 166:23-28.
 45. Ji GY, Oh CH, Won KS, Han IB, Ha Y, Shin DA, Kim KN. Randomized controlled study of percutaneous epidural neuroplasty using racz catheter and epidural steroid injection in cervical disc disease. *Pain Physician* 2016; 19:39-48.
 46. Manchikanti L, Bakhit CE. Percutaneous lysis of epidural adhesions. *Pain Physician* 2000; 3:46-64.
 47. Manchikanti L, Pampati V, Fellows B, Rivera J, Beyer CD, Damron KS. Role of one day epidural adhesiolysis in management of chronic low back pain: A randomized clinical trial. *Pain Physician* 2001; 4:153-166.
 48. Yabuki S, Kawaguchi Y, Nordborg C, Kikuchi S, Rydevik B, Olmarker K. Effects of lidocaine on nucleus pulposus-induced nerve root injury: A neurophysiologic and histologic study of the pig cauda equine. *Spine (Phila Pa 1976)* 1998; 23: 2383-2389.
 49. Yabuki S, Kikuchi S. Nerve root infiltration and sympathetic block. An experimental study of intraradicular blood flow. *Spine (Phila Pa 1976)* 1995; 20:901-906.
 50. Franson RC, Saal JS, Saal JA. Human disc phospholipase A2 is inflammatory. *Spine (Phila Pa 1976)* 1992; 17:S129-132.
 51. Ozaktay AC, Cavanaugh JM, Blagojev DC, King AI. Phospholipase A2 induced electrophysiologic and histologic changes in rabbit dorsal lumbar spine tissues. *Spine (Phila Pa 1976)* 1995; 20:2659-2668.
 52. 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 (Phila Pa 1976)* 1998; 23:1191-1196.
 53. Slipman CW, Huston CW, Shin C. Diagnostic and therapeutic injections. In: Gonzalez EG, Myers SJ, Edelman JE, Lieberman JS, Downey JA (eds). *Downey & Darling's Physiological Basis of Rehabilitation Medicine*. Butterworth Heinemann, Boston, MA, 2001, pp 795-813.

