Efficacy of Caudal Epidural Steroid Injection with Targeted Indwelling Catheter and Manipulation in Managing Patients with Lumbar Disk Herniation and Radiculopathy: A Prospective, Randomized, Single-Blind Controlled Trial

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■ BACKGROUND: **Lumbar disk herniation (LDH) is considered a common cause of lumbosacral radiculopathy. Epidural steroid injection is a common method to treat inflammation associated with low back–related leg pain. Spinal manipulations are widely used, and systematic reviews have also shown that these manipulations are more effective than placebos.**

■ OBJECTIVE: **Due to the absence of clinical evidence, we designed a prospective, randomized, single-blind controlled trial in patients with LDH with radiculopathy, aiming to detect the safety and clinical efficacy of targeted indwelling catheter combined with "4-step" manipulative therapy in patients with LDH.**

■ METHODS: **Patient visits were performed at baseline and days 1, 3, 7, and 28 after treatment. Clinical outcomes were measured using visual analog scale for back and leg pain, Oswestry Disability Index (ODI), and clinical symptom scores of the Japanese Orthopedic Association (JAO).**

■ RESULTS: **The study included 85 eligible patients. They were categorized with a randomization schedule into a Catheter Group ($N = 43$) and No-Catheter Group ($N = 42$). Between the measurement points, there was a statistically significant difference in the visual analog scale (back) at days 1, 3, and 7 of follow-up after treatment between the 2 groups. The change was statistically different at days 1 and 3, and a higher change was observed in the Catheter Group compared with the No-Catheter Group. There was a statistically significant difference in change of JOA and ODI scores at day 1 of follow-up after treatment between the 2 groups, and a greater change was seen in the Catheter Group at days 1 and 3 compared with the No-Catheter Group.**

■ LIMITATIONS: **The small sample size was small, and the follow-up time was short. The study also lacked documents of adjuvant therapies, like individual patient exercise routines and analgesic drug therapy.**

■ CONCLUSION: **Both methods were effective in reducing pain intensity and functional disability compared with pretreatment. The Catheter Group showed a more significant decrease in visual analog scale and greater changes in JOA and ODI scores of short/term follow-up, compared with the No-Catheter Group. The therapy project was safe.**

BACKGROUND

Lumbosacral radiculopathy, developing from compression of ≥1 spinal nerve roots, is characterized by radiating leg pain, leg paresthesia, and neurologic impairment.[1] Lumbar disk herniation (LDH), defined as localized disk displacement beyond the margins of the intervertebral disk space, is considered a common cause of lumbosacral radiculopathy.[2–5]

Conservative interventions include advice, medication, traction, manipulation, stabilization exercise, physical therapy, laser, ultrasound, and corsets. Among various procedural interventions for LDH, epidural steroid injection (ESI) is a common method to

Key words
- Epidural steroid injection
- Lumbar disk herniation
- Orthopaedic Association
- Oswestry Disability Index

Abbreviations and Acronyms
ESI: Epidural steroid injection
LDH: Lumbar disk herniation
ODI: Oswestry Disability Index
VAS: Visual analog scale

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treat inflammation associated with low back—related leg pain. In both conditions, the spinal nerves become inflamed due to the narrowing of passages through which the nerves pass down or out of the spine.[6] With the development of diagnosis and treatment technology, various epidural injection methods have been invented in clinical practice. There are 3 common approaches for delivering steroids into the epidural space: caudal, interlaminar, and transforaminal. In 2016, North American Spine Society specifically recommended that ESI of lumbar intervertebral disk herniation as a choice of grade A.

Caudal ESI, often simply referred as "epidural injection," places the needle through the sacral hiatus (a small boney opening just above the tailbone) to the bottom of the epidural space, delivering the steroid over a wider area. With the caudal approach, the steroid can spread over several spinal segments and cover both sides of the spinal canal. There are also some disadvantages, such as difficulties placing the needle into the sacral hiatus, getting close to the target disk herniation, and directly injecting steroid into the affected area near the nerve root inflammation lesions. In this study, we advanced caudal ESI therapy with a targeted indwelling catheter placed into the epidural space for several years.

Currently, the efficacy of some medical interventions is conflicting.[7] Spinal manipulations are widely used, and systematic reviews have also shown that these manipulations are more effective than placebos.[8-10] Much evidence shows that moderate manipulation is more effective than sham manipulation that generates back and leg pain.[11] The manipulation rationale includes reduction of a bulging disk, correction of disk displacement, release of adhesive fibrosis surrounding prolapsed disks or facet joints and entrapped synovial folds or plicae, inhibition of nociceptive impulses, relaxation of hypertonic muscles, and unbuckling displaced motion segments.[12]

In recent years, we have explored a unique method to treat LDH with radiculopathy. All patients in our institution received the "4-step" manipulative therapy (stretch, oblique pull, pull hip flexion knees, and shaking the waist) combined with cauda epidural steroid injections with targeted indwelling catheter.

Due to the absence of clinical evidence, we designed a prospective, randomized, single-blind controlled trial in patients with LDH with radiculopathy, aiming to detect the safety and clinical efficacy of this new technology.

MATERIALS AND METHODS

Study Design

The study was a prospective, randomized, single-blind, controlled trial. The study was conducted in accordance with the principles of the Declaration of Helsinki.[13] Approval to perform the study was obtained from the ethics committee. Each participating center has obtained Institutional Review Board approval. All the participants signed informed consents before the study.

Participants

Inclusion Criteria. Inclusion criteria included 1) patients aged 18—70 years, 2) complaints of radiating leg pain, 3) correlative imaging findings of structural degenerative pathology, and 4) ability to read, speak English or Chinese, study requirements and willingness to cooperate with the study instructions.

Exclusion Criteria. Exclusion criteria included 1) facet joint pain, 2) previous lumbar surgery, 3) pathologic cause of spinal disease, 4) any extraspinal cause of back pain, 5) structural spinal deformities (scoliosis >40°, spondylolisthesis), 6) nonspecific cause of back pain, and 7) unwillingness or inability to participate in follow-up procedures.

Recruitment. Participants were recruited through advertisements on bulletin boards and websites of local medical centers. All patients were screened initially by baseline assessment with regard to selection criteria before randomization. If inclusion criteria were met and the informed consent form was signed, the patient was sent to randomization.

Intervention. Eligible patients were randomized into 2 groups: targeted indwelling catheter ESI and traditional ESI. All the treating physicians were trained before this study. The trial was single-blind: Patients, investigators, and statisticians were unaware of treatment assignment. All procedures were performed under the guidance of C-arm fluoroscopy in the operating room. Patients were placed in prone position on a radiolucent table under all aseptic precautions and received a preservative-free local anesthetic, 0.5% lidocaine. A needle was advanced into midline epidural space using the loss of resistance technique. We gave an injection into the sacral hiatus of patients in prone position with a pillow. A pelvis needle was introduced through the sacrococcygeal ligament into the epidural space under fluoroscopic guidance to confirm epidural flow of injection before drug injection.[14] A combination of 10 mg triamcinolone acetate, 40 mL normal saline, and 5 mL lidocaine was injected. The position and injection procedures of our ESI with targeted indwelling catheter were same as traditional ESI, except that an indwelling catheter within the needle was gently inserted into the epidural space. Then we injected the drug (**Figure 1**).

Additional Interventions. All patients received 4-step manipulative therapy: stretching, oblique pull, pulling flexion knees, and shaking the waist. We concluded that this 4-step manipulative therapy can give a better dispersion of the drugs in the epidural space (**Figure 2**).

Outcomes. Patient visits were performed at baseline and days 1, 3, 7, and 28 after treatment. Clinical outcomes were measured using the visual analog scale (VAS) for back and leg pain, Oswestry Disability Index (ODI), and clinical symptom scores of Japanese Orthopaedic Association (JOA). VAS has a horizontal, 100-mm-long line, with "no pain" recorded on the left side (score: 0) and "pain as bad as it could be" on the right side (score: 10). Patients were asked to place a hatch mark on the line that corresponded to their current level of pain. The VAS score was then determined by measuring the millimeters between the left end point and the point that the patient marked.[15]

Sample Size. The sample size was calculated on the basis of previous significant pain relief. In a previous study, the VAS was reduced by 35.7 mm. Considering a 0.05 two-sided significance level in each group in both trials, a power of 80%, and an allocation ratio of 1:1, 39 participants in each group were

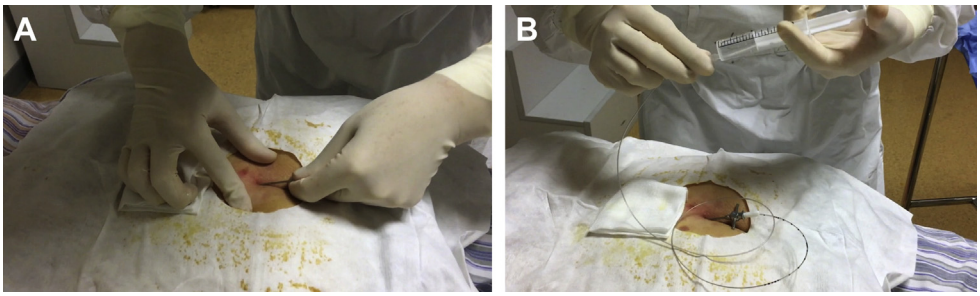

Figure 1. (**A** and **B**) Special technique of epidural steroid injection with a targeted indwelling catheter.

estimated. Allowing for a 20% attrition/noncompliance rate, a total of 90 participants with 45 participants in each group were included.[16]

Randomization. Site-specific randomization lists will be computer generated (i.e., generated by an individualized basic visual code program) and concealed from researchers by a senior data manager who was not involved in the study. This trial used a prospective, randomized, outcome-blinded design, in which all outcome assessments were made by a research assistant blind to treatment allocation and patient information. Forty-five participants selected from 90 were randomly assigned into each group.

Allocation Concealment. Patient randomization was done by another coordinator, without knowledge of physicians and participants. In the Catheter Group, the assigning was blind to participants and intervention performers. Participants were mixed with routine treatment participants. A statistician uninvolved with patient care assembled the data. Blinding was not interrupted because physicians and participants did not know the unblinding results.

Statistical Analysis

The statistical analysis was performed by a statistician blind to allocation. SPSS 20.0 statistical software (SPSS Inc., Chicago, Illinois, USA) was used for the statistical analysis. Mean, standard deviation, median, quartiles and interquartiles for continuous variables, and frequency for categorical variables were calculated. The Pearson chi-square (χ^2) test was used to compare the qualitative variables. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess normally distributed variables. The

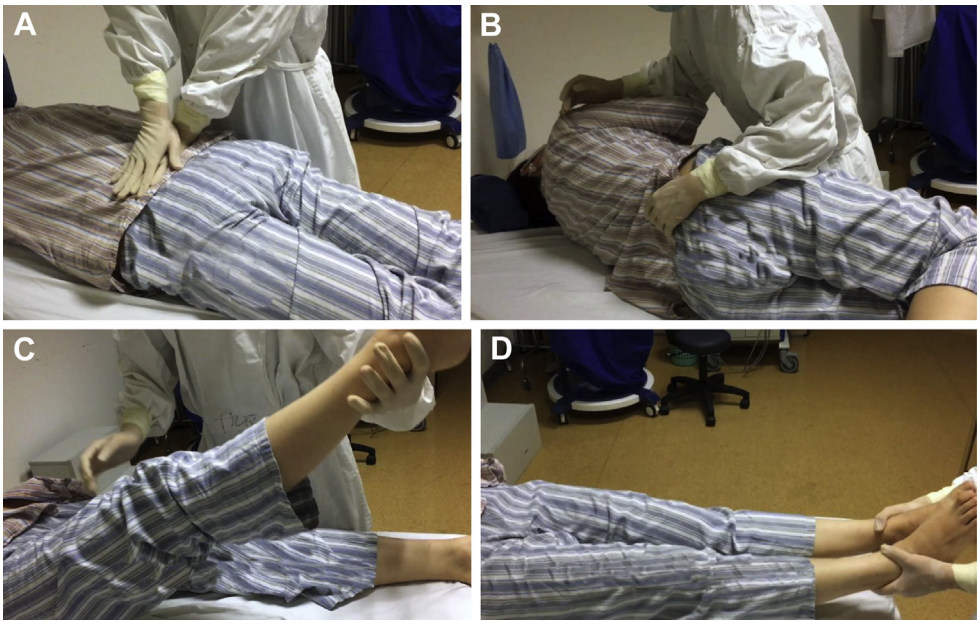

Figure 2. (**A**–**D**) Four-step manipulative therapy: stretch, oblique pull, pull hip flexion knees, and shaking the waist.

Mann-Whitney U test was used to compare the groups, whereas the Friedman test was used for multiple time point comparisons. In case of significant differences, least significant differences and Tukey honest significant difference tests were used to identify the time point(s) responsible for such differences. A P value <0.05 was considered significant.

An intent-to-treat analysis, which was performed after a sensitivity analysis in the original trials, was carried forward.

Quality Control

Before the trial, all staff involved were trained to know patient inclusion and exclusion, data collection, and intervention methods. During the trial, supervisors checked on case report forms and intervention. Dropouts, withdrawals (and the reasons), and the compliance of all patients were recorded in detail throughout the treatment and follow-up period.

Safety Assessments

All subjects were questioned about adverse events during the treatment at each visit, and all adverse events were analyzed, regardless of the investigators' assessments of causality. Safety was assessed by complete blood cell count, erythrocyte sedimentation rate, and blood chemistry.

RESULTS

Patient Demographic and Clinical Characteristics

Database records of patients treated in our institution for symptomatic lumbar disk herniation between April 2016 and March 2017 were prospectively collected and analyzed. Of the 88 eligible patients, 3 did not fulfill the inclusion criteria. The remaining 85 eligible patients and their 4 weeks' follow-up at our institute were included in the study. They were categorized with a randomization schedule into the Catheter Group (43 patients, 50.6%) and No-Catheter Group (42 patients, 49.4%), respectively. Among these patients were 42 males and 43 females, and the mean age was 55.2 years (range, 26–68 years). The mean duration of symptoms was 42.3 months (range, 1–240 months). The baseline scores at presentation for VAS (back), VAS (leg), JOA, and ODI were collected and analyzed. Table 1 summarizes the demographic and clinical characteristics. All the characteristics had no statistical significance (P > 0.05).

Between the measurement points, there was a statistically significant difference in the VAS (back) at days 1, 3, and 7 of follow-up after treatment between the 2 groups (P < 0.05). But there was not a statistically significant difference at day 28 of follow-up. Furthermore, the change was statistically different at days 1 and 3, and a higher change was observed in the Catheter Group compared with the No-Catheter Group (Table 2).

There was no statistically significant difference in the VAS (leg) at any time points after treatment between the 2 groups (P > 0.05). The change was statistically different at days 1 and 3, and a higher change was observed by the Catheter Group as compared with the No-Catheter Group (Table 3).

There was a statistically significant difference in change of JOA scores at day 1 of follow-up after treatment between the 2 groups (P < 0.05). But there was not a statistically significant difference at any other time point of follow-up. A greater change was seen in the Catheter Group at days 1 and 3 compared with the No-Catheter Group (Table 4).

There was a statistically significant difference in change of ODI scores at day 1 of follow-up after treatment between the 2 groups (P < 0.05). But there was not a statistically significant difference at any other time point of follow-up. A greater change was also seen in the Catheter Group at days 1 and 3 compared with the No-Catheter Group (Table 5).

Table 1. Demographic and Clinical Characteristics

	Group A (n = 43)	Group B (n = 42)
Age (mean ± SD) years	55.18 ± 12.51	55.19 ± 12.28
Gender: male	28	14
Smoker	4	4
Duration of symptoms(months)	45.55 ± 78.01	35.78 ± 66.60
VAS (back)	4.39 ± 2.64	4.88 ± 2.15
VAS (leg)	6.42 ± 2.01	6.72 ± 2.05
JOA	12.12 ± 4.32	10.77 ± 3.37
ODI	27.33 ± 7.88	27.51 ± 6.30
Level		
L3/L4	10	10
L4/L5	16	18
L5/S1	17	16
Motor deficits	11	14
Neurogenic claudication	1	1

SD, standard deviation; VAS, visual analog scale; JOA, Japanese Orthopaedic Association; ODI, Oswestry Disability Index; SD, standard deviation.

DISCUSSION

Transforaminal ESI, also known as "nerve block," places a needle alongside the nerve as it exits from the spine and injects medication into the "nerve sleeve." The medication then travels up the

Table 2. Comparison of Visual Analog Scale (Back) Between Groups and within Groups

VAS (Back)	Group C (n = 43)	Group N (n = 42)	*P* Value
Baseline	4.39 ± 2.64	4.88 ± 2.15	0.350
1 day	2.22 ± 1.44	3.41 ± 1.70	0.001*
3 days	2.00 ± 1.32	2.86 ± 1.39	0.005*
7 days	2.02 ± 1.41	2.69 ± 1.54	0.042*
28 days	2.50 ± 2.16	3.11 ± 1.73	0.150

Group C, epidural steroid injection (ESI) with targeted indwelling catheter; Group N, ESI not with targeted indwelling catheter.
*There was a statistically significant difference, $P < 0.05$.

Table 3. Comparison of Visual Analog Scale (Leg) Between Groups and within Groups

VAS (Leg)	Group C (n = 43)	Group N (n = 42)	*P* Value
Baseline	6.42 ± 2.01	6.72 ± 2.05	0.491
1 day	3.34 ± 1.81	4.00 ± 1.69	0.088
3 days	3.17 ± 1.88	3.65 ± 1.73	0.232
7 days	2.73 ± 1.94	3.60 ± 2.05	0.052
28 days	3.33 ± 2.72	4.30 ± 2.33	0.081

Group C, epidural steroid injection (ESI) with targeted indwelling catheter; Group N, ESI not with targeted indwelling catheter.

Table 5. Comparison of Oswestry Disability Index (ODI) Between Groups and within Groups

ODI	Group C (n = 43)	Group N (n = 42)	*P* Value
Baseline	27.33 ± 7.88	27.51 ± 6.30	0.908
1 day	19.40 ± 7.47	22.84 ± 6.38	0.025*
3 days	17.14 ± 8.46	20.26 ± 6.63	0.062
7 days	15.79 ± 9.59	18.81 ± 6.90	0.098
28 days	15.19 ± 11.25	18.77 ± 8.90	0.107

Group C, epidural steroid injection (ESI) with targeted indwelling catheter; Group N, ESI not with targeted indwelling catheter.
*Statistically significant difference, $P < 0.05$.

sleeve and into the epidural space from the side. Transforaminal ESI can be modified better recovery. Caudal approach ESI, often referred as "epidural injection," places the needle into the epidural space through the sacral hiatus, dispersing the steroid to a wider area. With the caudal approach, the medication can be spread over several spinal segments and both sides of the spinal canal. In the clinical work, we found some disadvantages of traditional caudal approach ESI, evidenced by the difficulties of placing the needle into the sacral hiatus, getting close to the target disk herniation, and directly injecting steroid into the affected area near the nerve root inflammation lesions. Therefore we modified the traditional caudal ESI with a targeted indwelling catheter placed into the epidural space.

Spinal manipulations are widely used.[17] Evidence shows that manipulations are effective for relieving back and leg pain at short and intermediate follow-ups in patients with LDH.[11] Systematic reviews have also shown that manipulations are more effective than placebo for pain relief.[12] In this review, 3 trials compared the efficacy of manipulations of different therapies.[11,18,19]

After years of clinical work, we have developed a unique manipulation therapy program including stretching, oblique pull, pulling hip flexion knees, and shaking the waist. We therefore conducted a prospective, randomized, single-blind controlled trial to assess the safety and short-term impact of caudal ESI with a targeted indwelling catheter combined with the "4-step" manipulative therapy in a cohort of patients with lumbar disk herniation with radiculopathy.

Table 4. Comparison of Japanese Orthopaedic Association (JOA) Between Groups and within Groups

JOA	Group C (n = 43)	Group N (n = 42)	*P* Value
Baseline	12.12 ± 4.32	10.77 ± 3.37	0.111
1 day	17.93 ± 4.83	15.58 ± 3.67	0.013*
3 days	18.50 ± 4.78	17.37 ± 3.18	0.203
7 days	20.05 ± 5.20	18.26 ± 3.71	0.071
28 days	19.00 ± 6.80	17.05 ± 5.33	0.144

Group C, epidural steroid injection (ESI) with targeted indwelling catheter; Group N, ESI not with targeted indwelling catheter.
*Statistically significant difference, $P < 0.05$.

Our study revealed that the caudal approach can effectively relieve pain in patients with LDH with lumbosacral radicular pain, compared with the traditional approach. Our analysis indicated that 2 methods effectively reduced pain intensity (VAS) and functional disability (JOA and ODI scores) compared with pretreatment, which is consistent with other literature.

While short-term impacts on pain intensity and functional disability were comparable between 2 groups, the Catheter Group showed a more significant decrease in VAS (back and leg) at days 1 and 3 of follow-up and greater JOA and ODI scores at day 1 of follow-up, compared with the No-Catheter Group. And the study showed there was no significant difference in pain intensity and functional disability at days 7 and 28 of follow-up. For the Catheter Group, more accurate delivery of local steroid in a wider area with targeted indwelling catheter brought this improvement. But this improvement had no difference between the 2 groups 30 minutes or 1 hour after injection. Furthermore, it is much more convenient and quick with targeted indwelling catheter compared with the other group, indicating that convenience was mainly because an indwelling catheter makes it easier to place the needle into the sacral hiatus.

ESI have been performed for many decades. Serious complications are rare, except for allergic reaction, bleeding, infection, nerve damage, or paralysis. If performed by an experienced physician using fluoroscopic guidance, the risk of serious complications is minimized. In our clinical work and the study, there have been no adverse events and complications, so we generally consider this technology to be a safe, effective treatment for LDH with radiculopathy.

The factors contributing to its success include high internal validity; effective masking of interventionalists, patients, and assessors; consistent retention of patients throughout the study; and adequate sample size for a well-powered equivalence trial.

This study had some limitations. First, the small sample size had an impact on the accuracy of some parameters, but it was

adequate to evaluate the variables. Second, the study was inherent to a prospective review of clinical data, although most factors are similar to those in other prospective studies. The therapeutic parameters, physical examination signs, and imaging studies would not have differed if the study had been set up as a prospective study. Third, the follow-up time is only 28 days. Owing to the lack of long-term follow-up, its long-term efficacy remains unknown. Fourth, it lacks documents of adjuvant therapies, like individual patient exercise routines and analgesic drug therapy.

CONCLUSION

We conducted a prospective, randomized, single-blind controlled trial to assess the efficacy of caudal ESI with a targeted indwelling catheter combined with "4-step" manipulative therapy for patients with LDH. Both methods were effective in reducing pain intensity (VAS) and functional disability (JOA and ODI scores) compared with pretreatment. And the Catheter Group showed more significant decrease in VAS (back and leg) and greater changes in JOA and ODI scores of short/term follow-up, compared to with the No-Catheter Group. The therapy project was safe.

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