

Evaluation of lung function and clinical features of interlaminar cervical epidural steroid injections: a randomized controlled trial

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Abstract

Objective: Interlaminar cervical epidural steroid injections (ICESIs) are commonly used to treat axial neck pain and cervical radicular pain. However, local anesthetics can spread to and block the phrenic nerve and upper segments of the thoracic spinal cord where the sympathetic innervation of the lungs emerges. Therefore, changes in lung function may occur following ICESIs.

Methods: The primary outcome measure was the pulmonary function test (PFT) result 30 minutes before and after ICESI with ropivacaine (0.1875% or 0.25%). The secondary outcome measure was the comparison of the pain scores and functional disability between the two concentrations of ropivacaine 4 weeks after the ICESIs.

Results: Fifty patients were randomly assigned to either the R1 (0.1875% ropivacaine) or R2 (0.25% ropivacaine) group. No significant difference was observed between the pre-ICESI and 30-minute post-ICESI PFT results within each group, and no difference was observed between the two groups. After 4 weeks of treatment, both groups showed a significant decrease in pain scores and functional disability; however, no significant differences were observed between the two groups.

Conclusions: This study showed no significant change in lung function after ICESIs in either group and no local anesthetic concentration-based difference in the clinical efficacy of the ICESIs.

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Introduction

Interlaminar cervical epidural steroid injections (ICESIs) are commonly used to treat axial neck pain and cervical radicular pain.¹ Although the long-term effectiveness of ICESIs is controversial, ICESIs are an effective treatment option for patients who are unable or unwilling to undergo surgical interventions.²

Although there is a consensus across disciplines that ICESIs are safe, the complication rate is considered to be higher in the cervical spine than in the lumbar spine.³ The reported complication rates associated with ICESIs range from 0.0% to 16.8%.⁴ Complications of ICESIs range from minor effects to death,⁴ and one possible complication is respiratory insufficiency.⁵ Although respiratory compromise is rare,⁴ it can occur in patients with lung disease or advanced age.^{5,6}

When performing ICESIs, the local anesthetics (LAs) can spread to approximately five vertebral segments in both the cephalad and caudad directions.⁷ Accordingly, LAs can block the phrenic nerve (C3–C5) and the upper segments of the thoracic spinal cord where the sympathetic innervation of the lungs emerges. Sympathetic neurons that innervate the lungs are located in the stellate ganglia and T2–T4 sympathetic chain ganglia.^{8,9}

In ICESIs, low-concentration LAs are used to alter the nociceptive process, resulting in excess release of neurotransmitters, nociceptive sensitization of the nervous system, and phenotype changes.¹⁰

However, low-concentration LAs do not block motor nerve fibers. Accordingly, many pain physicians believe that lung function will not change after ICESIs. However, many studies have revealed a decrease in lung function despite the use of low-concentration LAs in various blockades performed in the cervical region.^{11–14}

Although these results cannot be directly applied to ICESIs, we hypothesized that low-concentration LAs can decrease lung function by blocking the upper thoracic spinal cord and phrenic nerve, even in ICESIs. To the best of our knowledge, no studies have evaluated lung function in patients undergoing ICESIs. Therefore, our primary objective in the present study was to evaluate the changes in pulmonary function test (PFT) results in patients undergoing ICESIs using common low-concentration LAs (ropivacaine 0.1875% or 0.25%),^{15–17} and our secondary objective was to compare the clinical efficacies (pain scores and functional disability) of different concentrations of LAs.

Materials and methods

This randomized controlled trial was approved by the institutional review board of Ewha Womans University Mokdong Hospital (EUMC 2019-04-031-011) and is registered with the Clinical Research Information Service (registration number: KCT0004343). This study was conducted according to the tenets of the Declaration of Helsinki. Written consent for

participation was obtained from all patients before enrollment in the study group. The reporting of this study conforms to the CONSORT statements.¹⁸

Randomization and blinding

Fifty patients were enrolled and randomly assigned (1:1) to either the R1 group (0.1875% ropivacaine) or R2 group (0.25% ropivacaine) using a computer-generated randomization schedule. The random numbers were kept in a sealed location and opened by a pain nurse who was not involved in this study. Sterile syringes containing two concentrations of ropivacaine (0.1875% or 0.25%) were prepared in a double-blind manner by a pain nurse. All procedures were performed by the corresponding author (KWJ), who was blinded to the concentrations of the administered injectates, and a resident, who was blinded to the study objectives.

Participants

The inclusion criteria were (a) an age of 20 to 70 years; (b) herniated nucleus pulposus and/or cervical stenosis after a series of physical, neurological, and magnetic resonance imaging examinations; (c) no therapeutic ICESIs within the previous 6 months; (d) a pain intensity score of ≥ 4 on a numeric rating scale (NRS) (0: no pain, 10: worst pain imaginable) during the conservative treatment period; and (e) no prior surgery. The exclusion criteria were (a) refusal to participate, (b) pregnancy, (c) cognitive impairment, (d) coagulation disorder, (e) acute infection, (f) long-term oral steroid therapy, (g) allergy to contrast media or LAs, (h) neuromuscular disorder, and (i) cardiopulmonary disorders, including a history of lung disease or lung surgery.

Procedures

To prepare for an emergency, an intravenous route was secured before the procedure, and vital signs were monitored during the procedure. The patients were placed in the prone position on a table, disinfected with betadine, and draped. After confirming the insertion point (C7/T1) of the needle with the anteroposterior (AP) view, a 22-gauge Tuohy needle was inserted ipsilaterally in the lesion through a paramedian approach using the AP view (Figure 1 (a)). The needle was advanced while monitoring the depth using the lateral view until it reached the spinolaminar line. Once the needle reached the spinolaminar line, the epidural space was identified using the loss-of-resistance technique (Figure 1(b)). When loss of resistance was confirmed, 1 mL of contrast medium was injected using real-time images to confirm the epidural space in the AP view (Figure 1(c)) and lateral view (Figure 1(d)); the absence of intravascular, subarachnoid, or extra-epidural injections was also confirmed. Next, 5 mL of 0.1875% or 0.25% ropivacaine with 5 mg of dexamethasone was injected into the epidural space.

Outcome measures

The primary outcome measure was lung function. The PFTs were performed with the patients resting in a sitting position 30 minutes before and after the ICESIs. The PFTs included forced vital capacity, forced expiratory volume in 1 second, and peak expiratory flow rate measured using a spirometer (Pony Fx; COSMED Srl, Rome, Italy). A well-fitted mouthpiece was used to prevent air leakage, and the patient's nose was closed using a nose clip. PFTs were performed twice for each patient, and the test with the more accurate value was selected.

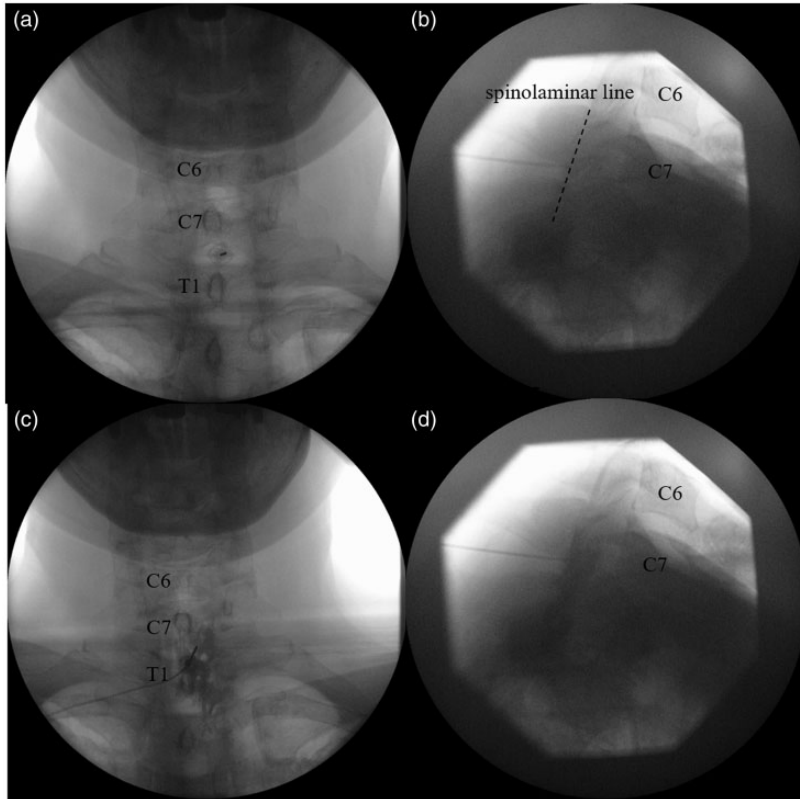


Figure 1. Interlaminar cervical epidural steroid injection procedure.

(a) Needle positioned at the C7/T1 interlaminar space. (b) Pre-contrast needle positioned near the spinolaminar line. (c) Anteroposterior fluoroscopic image with 1 mL of contrast medium and (d) Lateral fluoroscopic image with 1 mL of contrast medium.

The secondary outcome measures were pain scores and functional disability. The intensity of neck and radicular pain was evaluated using the NRS, and functional disability was evaluated using the Korean version of the Neck Disability Index (NDI) (score range, 0–50).¹⁹ In addition, data related to each patient's age, sex, height, weight, hypertension, diabetes mellitus, pain duration and location, treatment history (including the Medication Quantitative Scale (MQS) score), and etiology were collected. The MQS was used to quantify the patients' medications. An MQS score was calculated for each pain-related medication based on weights

assigned by pharmacologic class and dosage level; these scores were summed to calculate the total MQS score.²⁰ Sensory changes were evaluated based on pinprick and cold sensations (0: absent, 1: altered, and 2: normal), and motor weakness was evaluated using a 5-point scale (0: no contraction to 5: normal strength) 30 minutes after the procedure. Adverse effects were also noted.

Statistical analysis

To examine the validity of the study, a power analysis for sample size estimation was performed using G*Power, version 3.1

(Heinrich Heine University, Düsseldorf, Germany). We calculated the sample size based on data from a previous study.²¹ Fifty patients (23 per group, dropout rate: 10%) were determined to be necessary with a power of 0.95 and an α value of 0.05.

The Shapiro–Wilk test was used to examine the normality of continuous variables. Continuous variables are expressed as mean \pm standard deviation or median (interquartile range), and categorical variables are presented as numbers. Demographic data, changes in PFT results, pain scores, and functional status were analyzed using Student's *t*-test, the Mann–Whitney U test, the chi-square test, the paired *t*-test, or the Wilcoxon signed-rank test, as appropriate. Two-sided *p*-values of <0.05 were considered statistically significant. All statistical analyses were performed using PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

From August 2019 to September 2021, 50 patients were randomized into the R1 or R2 group. One patient in the R1 group and two patients in the R2 group were lost to follow-up (Figure 2). The basic characteristics of the two groups are shown in Table 1. No statistically significant differences were observed between the groups.

The PFT results of each group are shown in Table 2. No significant difference was observed between the pre-ICESI and 30-minute post-ICESI PFT results within each group (Table 2), and no difference was observed between the two groups (Table 3).

Moreover, no significant differences in the baseline NRS scores for neck and radicular pain or the NDI scores were observed between the two groups. After 4 weeks of treatment, both groups showed significant

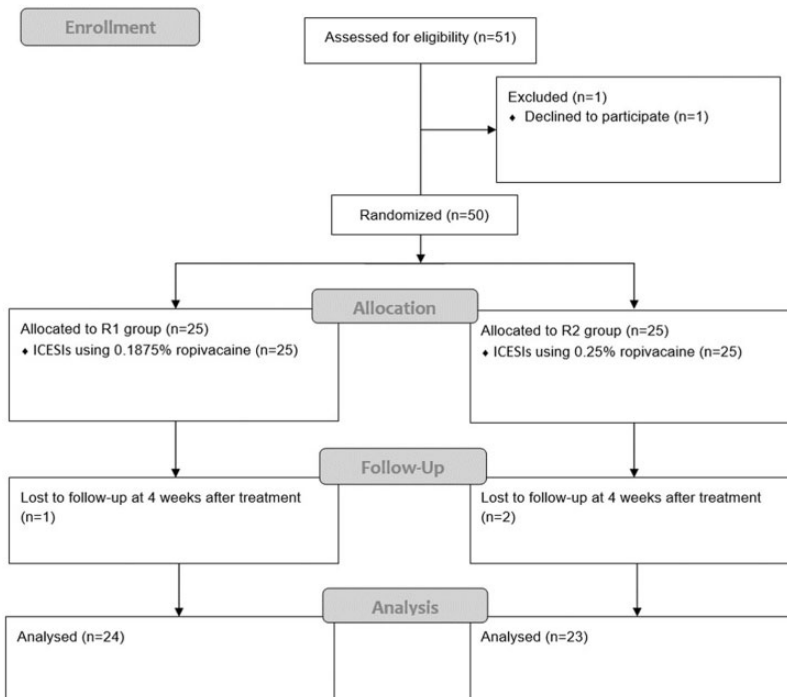


Figure 2. Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

Table 1. Demographic data.

Variables	R1 group (n = 24)	R2 group (n = 23)	p-value
Age, years	52.5 ± 9.6	54.7 ± 9.5	0.445
Sex, M/F	12/12	11/12	0.882
Height, cm	162.4 ± 7.8	165.6 ± 8.5	0.182
Weight, kg	63.8 ± 11.9	64.0 ± 10.3	0.939
Hypertension	5	4	0.764
Diabetes mellitus	3	2	0.672
Pain duration, months			
0–3/3–6/6–12/ > 12	6/1/2/15	10/1/1/11	0.587
Location of pain, left/right	10/14	13/10	0.308
Medication Quantification Scale score	5.4 ± 1.5	5.4 ± 1.4	0.953
Etiology			
HNP/spinal stenosis/spinal stenosis with HNP	10/0/14	10/0/13	0.900
Single level/multiple levels	2/22	3/20	0.601
Bulging/protrusion/extrusion/sequestration	2/19/3/0	1/21/1/0	0.493
Foraminal stenosis	14	13	0.900
Anterolisthesis or retrolisthesis	3	1	0.317

Values are presented as mean ± standard deviation or number of patients.

HNP, herniated nucleus pulposus; M, male; F, female.

Table 2. Lung function data.

Variable (% of predictive value)	R1 group (n = 24)	R2 group (n = 23)
FVC		
Pre-ICESI	101.00 (22.00)	98.78 ± 10.32
Post-ICESI	99.00 (22.50)	97.30 ± 10.76
p-value	0.966 [†]	0.582*
FEV1		
Pre-ICESI	99.08 ± 19.93	99.00 (26.00)
Post-ICESI	98.50 ± 17.16	94.00 (15.00)
p-value	0.850*	0.862 [†]
PEFR		
Pre-ICESI	81.67 ± 28.58	68.52 ± 29.01
Post-ICESI	81.46 ± 22.60	64.30 ± 25.21
p-value	0.959*	0.439*

Values are presented as mean ± standard deviation or median (interquartile range).

*Paired t-test, [†]Wilcoxon signed-rank test.

FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; PEFR, peak expiratory flow rate.

alleviation of neck and radicular pain according to the NRS scores ($p < 0.001$) and improvement in the functional status according to the NDI scores ($p < 0.001$).

In this regard, no significant differences were observed between the two groups (Figure 3).

No sensory changes or decreased motor function was observed in either group, and no serious adverse events occurred. No dural puncture or subdural or intrathecal injections occurred in either group. No patients in either group developed infectious complications, persistent paresthesia, systemic steroid reactions, skin lesions, or adverse reactions to contrast agents or adjuvants.

Discussion

In the present study, lung function did not change after ICESIs and did not differ between the two LA concentrations. Although pain scores and functional disability were significantly decreased after ICESIs, no significant difference was observed between the two groups.

When performing ICESIs, the needle insertion point is usually at C7/T1 because this site has the largest epidural space

Table 3. Changes in lung function.

Variable (% of predictive value)	R1 group (n = 24)	R2 group (n = 23)	p-value
Change in FVC	1.50 (11.00)	5.00 (13.00)	0.312 [†]
Change in FEV1	1.00 (11.75)	1.00 (14.00)	0.807 [†]
Change in PEFR	0.21 ± 19.73	4.22 ± 25.67	0.550*

Values are presented as mean ± standard deviation or median (interquartile range).

*t-test, [†]Mann–Whitney U test.

FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; PEFR, peak expiratory flow rate.

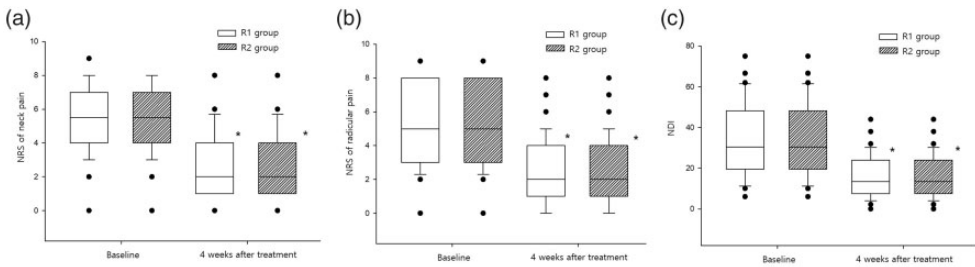


Figure 3. Pain scores and functional status outcomes. (a) NRS for neck pain. (b) NRS for radicular pain and (c) NDI. * $p < 0.001$ (pre-ICESI vs. post-ICESI; Wilcoxon signed-rank test).

NRS, numeric rating scale; NDI, Neck Disability Index.

relative to the dura and spinal cord in the cervical spine, thereby providing more room to work. Additionally, the cervical ligamentum flavum can fail to fuse, thus leaving gaps at all cervical levels; however, lower failure rates have been reported at the lower levels.²² In ICESIs, the volume of the injectate significantly affects its longitudinal spread in the epidural space. Generally, 2 to 10 mL of injectate is considered adequate for adults. Although many studies have examined the optimal injection volume when performing ICESIs, we selected 5 mL as the volume of the injectate because Lee et al.⁷ reported that the optimal volume for distributing epidural medications in patients with degenerative cervical diseases is 5 mL. In their study, the mean numbers of vertebral segments in the cephalad and caudad directions of the contrast agent were 5.5 ± 1.3 and 5.2 ± 3.6 , respectively.⁷ Therefore, the injectate could reach the

C3–C5 (phrenic nerve) level and the upper thoracic spinal cord where the sympathetic innervation of the lungs emerges.

Several studies have shown that the autonomic nervous system may be connected to the respiratory system because sympathetic neurons that innervate the lungs are located in the stellate ganglia and the T2–T4 sympathetic chain ganglia.^{8,9} LAs induce selective sympathetic, sensory, and motor blockade depending on the drug concentration²³; sympathetic nerve fibers are blocked more easily than any other fibers.²⁴ One study showed that after performing stellate ganglion block using low-concentration LAs, PFT indices were significantly decreased and paralysis of the diaphragm occurred,¹⁴ which can result from thoracic sympathetic blockade.¹⁴ Additionally, studies have demonstrated phrenic nerve blockade and decreased diaphragmatic function following

the administration of low-concentration LAs in the interscalene block.^{11–13} PFT indices (i.e., forced vital capacity, forced expiratory volume in 1 second, and peak expiratory flow rate) were reduced in both groups (ropivacaine 0.1% and 0.2%) compared with the baseline pre-block values.¹¹

Although the aforementioned results cannot be directly applied to this study, even in ICESIs, we hypothesized that low-concentration LAs can spread to and block the upper thoracic spine where the sympathetic innervation of the lungs emerges and that LAs spreading to the C3–C5 level can block the phrenic nerve, which can cause respiratory compromise. However, our results confirmed no changes in the PFT results. Although explaining this phenomenon is difficult, we consider that 5 mL of a low-concentration LA in ICESIs is unable to block the motor fibers of the phrenic nerve, resulting in the discrepancy in the results between the present study and previous studies.

It is important to note that applying our results to patients with lung disease or advanced age may not be safe. Moreover, our results may not be applicable if a high volume of injectate is used for ICESIs. An increased sensitivity to LAs, as in older patients, may be due to lower numbers of myelin fibers in the dorsal and ventral roots and increased permeability due to myelin sheath deterioration.⁶ Moreover, increasing the volume of LAs, even at low concentrations, is associated with further impairment of lung function in the interscalene block.^{25–27}

Our results showed that the NRS and NDI scores were not significantly different between the two groups. Few studies have examined the effects of LA concentrations on pain scores and functional disability. Bartynski et al.²⁸ evaluated the immediate pain response to lumbar epidural steroid injections using LAs and steroids (0.25%–0.5% bupivacaine). They found that the

effect was independent of the LA concentration used, which is consistent with the results of the present study.

This study has several limitations. First, it was conducted with only ropivacaine. Therefore, the findings cannot be extrapolated to other LAs. Second, we did not confirm epidural spreading. Third, we performed the PFTs with the patients in the sitting position only. Fourth, we enrolled a small number of patients, and the statistical power was inadequate to identify slight differences in the PFT results. Fifth, we did not analyze long-term outcomes. Sixth, we injected only one volume (5 mL).

Conclusion

No significant changes in lung function were observed in either group after ICESIs, and no difference in the clinical efficacy of ICESIs was found between the two LA concentrations. Large multicenter randomized controlled trials using high volumes of injectates in ICESIs are warranted to evaluate their effects on PFTs.

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Disclosure

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