

척추관 협착증 환자에서 경피적 경막외 신경성형술을 통한 스테로이드 단일 주입 및 지속적 투약의 효과 비교

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Epidural Neuroplasty with Single Bolus Injection versus Continuous Infusion of Steroid in Patients with Spinal Stenosis

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Objective: To compare the efficacy of epidural adhesiolysis with a single bolus steroid injection (EAS) and continuous steroid infusion (EAC). **Method:** Thirty-one patients were allocated to the EAS group (10 patients) and EAC group (21 patients). EAS received single bolus of 10 mg of dexamethasone. EAC received a total of 96 mL dexamethasone solution (20.0 mg of dexamethasone) for 48 hrs. Oswestry Disability Index (ODI) was evaluated before, one month after the procedure. Three months after the procedure, the Patient's Global Impression of Change (PGIC) was evaluated. **Results:** Pre-treatment ODI was 38.3 ± 3.1 in EAS and 46.40 ± 4.0 in EAC. One month later, ODI was decreased to 35.60 ± 3.33 , 43.08 ± 6.96 in each group ($p=0.174$). Three months later, 2 patients in the EAS (20.0%) and 8 patients in EAC (38.1%) showed 'much improvement' in PGIC, 5 patients in EAS (50.0%) and 6 patients in EAC (38.1%) showed 'slight improvement', 3 patients in EAS (30.0%) and 7 patients in EAC (33.3%) showed 'no improvement' ($\chi^2=1.588$, $p=0.510$). **Conclusion:** Epidural adhesiolysis with continuous infusion did not show any superiority than single bolus injection. (Clinical Pain 2018;17:74-80)

Key Words: Spinal Stenosis, Epidural Adhesiolysis, Corticosteroid, Continuous Infusion

INTRODUCTION

Spinal stenosis is a degenerative spine disease characterized by narrowed spinal canal due to a herniated intervertebral disc, ligamentum flavum thickening, and/or an enlarged facet joint.¹ Treatments for spinal stenosis have included oral medication, physical modalities, epidural steroid injection, and decompression surgery. All the non-surgical treatments provide only short-term symptom relief.² Even decompression surgery shows symptom recurrence due to instability caused by partial laminectomy or adjacent disc herniation caused by lumbar posterior

fixation.³

Recently, epidural adhesiolysis or neuroplasty has been used to treat lumbar spinal stenosis. Whether the therapeutic effect of epidural adhesiolysis is superior to conventional epidural steroid injection for lumbar spinal stenosis is still controversial.⁴⁻⁷ The mechanism by which epidural adhesiolysis achieves its benefit has not been determined, but proposed mechanisms have included washout of inflammatory cytokines by infused saline, mechanical adhesiolysis by the catheter tip, accurate drug delivery by the catheter, and osmotic pressure by hypertonic saline.⁴ Birkenmaier et al.⁸ suggests that the mechanism of neuroplasty is through a targeted application of epidural medications and a possible lavage effect rather than a mechanical lysis of scars or adhesions.

Epidural adhesiolysis can be performed with a single bolus injection or continuous steroid infusion. Continuous analgesic infusion into the epidural space is a well-known

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technique to control labor and postoperative pain. This technique was used in chronic lumbar radiculopathy refractory to conventional epidural injection, and an indwelling epidural catheter with an infusion pump showed a better effect.⁹ This result was thought to be due to injection of a larger volume, and a previous meta-analysis supports this assumption by demonstrating a positive correlation between volume of fluid injected in the epidural space and relief of radicular leg pain or low back pain.¹⁰ Larger volumes were suggested to evoke washout of inflammatory cytokines. Therefore, epidural adhesiolysis with continuous steroid infusion would be more effective for spinal stenosis than would epidural adhesiolysis with a single bolus steroid injection if the mechanism would be a washout of inflammatory cytokines. However, no study has compared epidural adhesiolysis with a single bolus steroid injection to epidural adhesiolysis with continuous steroid infusion for spinal stenosis.

Our hypothesis was that epidural adhesiolysis with continuous steroid infusion would be more effective than epidural adhesiolysis with a single bolus steroid injection because continuous infusion would wash out inflammatory cytokines. The aim of this study was to compare the efficacy of epidural adhesiolysis with continuous steroid infusion to that of epidural adhesiolysis with a single bolus steroid injection. Also, if epidural adhesiolysis is effective for pain relief of refractory spinal stenosis patient, we want to find out which patients are more suitable candidates of epidural adhesiolysis.

MATERIALS AND METHODS

Data was collected by retrospective chart review of patients with spinal stenosis treated with epidural adhesiolysis from January 2014 to March 2017. This study was approved by the Institutional Review Board (IRB) of Samsung medical center (IRB approval number: 2016-05-052). The selection criteria of the study subjects were adults older than 19 years who were diagnosed with spinal stenosis by MRI imaging and received a previous epidural steroid injection but had shown poor improvement and had not undergone spinal steroid injection within the past 3 months. Patients underwent blood testing including complete blood cell count, blood chemistry, and coagulation profile and were excluded if there were abnormalities in those results

and were excluded if were unable to obtain proper consent.

A total of 31 patients participated in the study. 15 patients received transforaminal epidural injection, 1 patients received caudal injection, 1 patients received interlaminar epidural injection, 14 patients received their combination, but did not know their injection type accurately. Spinal stenosis was diagnosed by clinical symptoms such as neurogenic claudication and lumbosacral magnetic resonance images (MRI). The grading of lumbar spinal stenosis was divided according to the grading system: grade 1: defined as mild lumbar central canal stenosis (LCCS), in which the anterior CSF space was mildly obliterated, but all cauda equina could be clearly separated from each other; grade 2: defined as moderate LCCS, in which the anterior CSF space was moderately obliterated and some of the cauda equina were aggregated, making it impossible to visually separate them; and grade 3: defined as severe LCCS, in which the anterior CSF space was obliterated so severely as to show marked compression of the dural sac, and none of the cauda equina could be visually separated from each other, appearing instead as one bundle.¹¹ Neurogenic claudication was defined as increasing radiating pain to the leg during walking or standing with lumbar extension and alleviated pain after resting or taking a flexed lumbar posture.¹² Lumbosacral MRI showed a central canal or foraminal narrowing caused by a herniated disc, ligamentum flavum hypertrophy, or bony spur.¹³

Patients who were recruited from January 2015 to August 2016 received epidural adhesiolysis with continuous infusion at inpatient ward (EAC group) and those recruited from September 2016 to March 2017 received epidural adhesiolysis with a bolus injection in outpatient clinics (EAS group). Epidural adhesiolysis with a bolus injection was done in an air-clean room, that contained a fluoroscope (Model: Artis Zee Ceiling, Siemens Medical Solutions, Erlangen, Germany). Patients lay on the table in the prone position. The skin of the coccyx area was sterilized with 1% chlorhexidine. After checking the sacral hiatus fluoroscopically, skin anesthetic (1% lidocaine solution) was injected into the sacral area. A 16-gauge Tuohy needle with stylet was inserted into the sacral hiatus and progressed to the S3 vertebral body. The stylet was removed, and a curved epidural catheter (Epistim[®], Sewoon Medical Corp., Seoul, Korea) was inserted (Fig. 1). The curved part was controlled to locate the catheter tip at the most stenotic

area (Fig. 2), which was confirmed with contrast dye (Iobrix[®], Taejoon Pharm Co. Ltd., Seoul, Korea). A single, 10-mg bolus of dexamethasone sodium phosphate (5 mg/mL; Yuhan Corp., Seoul, Korea) and 1,500 IU of hyaluronidase (H-lase[®], LNH Pharm, Seoul, Korea) mixed with 1 mL of ropivacaine HCl (Ropiva[®], Huons Co. LTD, Seongnam, Korea) was injected. The catheter was then removed, and the patient was discharged after 30 minutes rest.

Epidural adhesiolysis with continuous infusion was performed in the same space with the same procedure. Instead of removing the catheter after injection of dexamethasone, hyaluronidase, and ropivacaine, it was fixed with an adhesive patch and connected to an infusion pump. A total of 96 mL of dexamethasone solution (20.0 mg of dexamethasone mixed with 92 mL of normal saline) was slowly

infused over 48 hours at rate of 2 mL/hour. After the procedure, the catheter was removed, and the patient was discharged.

Patient-reported pain outcome was classified into three categories by using the Patient's Global Impression of Change (PGIC). 'Poor improvement' was defined as less than 30% improvement in subjective symptoms, 'slight improvement' was defined as 30-50% improvement, and 'much improvement' was defined as more than 50% improvement. These criteria were based on a previous study.¹⁴ The PGIC, and Oswestry Disability Index (ODI) were used to evaluate pain and disability before the procedure respectively.

The ODI were reevaluated one month after, and PGIC were reevaluated three months after discharge respectively to determine the effect of epidural adhesiolysis with a bolus injection or continuous infusion. Repeated measures of ANOVA were conducted to compare ODI changes one month after the procedure and the Chi-square test was used for differences in PGIC between groups.

The possible complications from epidural adhesiolysis with a bolus injection and continuous infusion including dural puncture, motor weakness, infection, and bleeding were investigated during the study period.

RESULTS

A total of 31 patients participated in the study with 10 (7 men and 3 women) undergoing epidural adhesiolysis with a bolus injection and 21 (7 men and 14 women) undergoing epidural adhesiolysis with continuous infusion. The average age was 64.2 ± 3.5 years in the EAS group and 66.19 ± 2.0 years in the EAC group ($p=0.604$). The average duration of symptoms was 19.50 ± 5.6 months in the EAS group and 15.25 ± 3.5 months in the EAC group

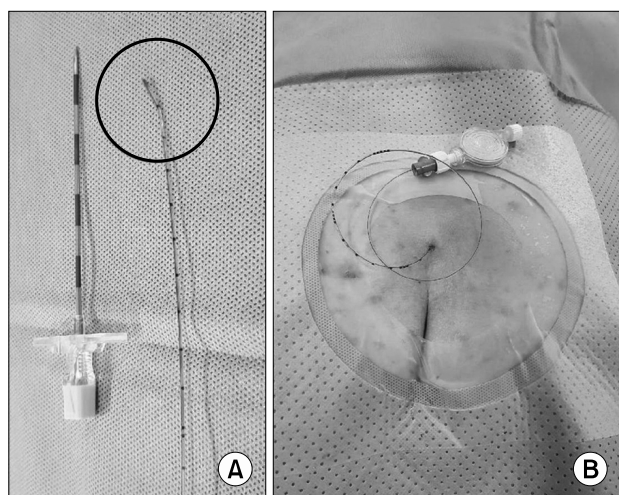


Fig. 1. (A) Curved epidural catheter was inserted into the sacral hiatus and approached to the most stenotic area by controlling the direction of the curved part (red circle). (B) Catheter was positioned, and dexamethasone solution was injected.

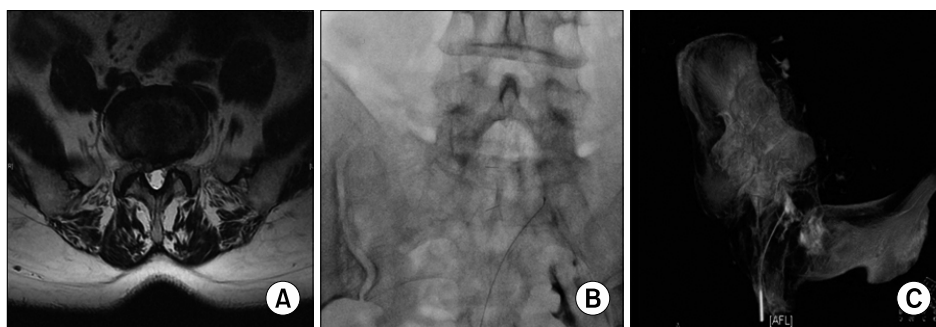


Fig. 2. (A) Patient's Lumbosacral MRI image shows lateral foraminal spinal stenosis. (B) The epidural catheter was inserted, and the curved part was controlled to locate the catheter tip at the most stenotic area in the MRI images. (C) This was confirmed with contrast dye by 3D constructed computed tomographic images.

($p=0.524$). 9 patients in EAS group (9/21, 42.85%) and 1 patient in EAS group (1/10, 10.00%) had a history of lumbar surgery. ($p=0.106$). All patients had previously had at least one epidural injection. The EAS group had an average of 2.7 ± 0.7 previous epidural injections and the EAC group had 4.5 ± 0.8 ($p=0.164$). Based on MRI findings, there are no differences in spinal stenosis grade between EAC group (Grade 1: 4, grade 2: 9, grade3: 8, 1.33 ± 0.20) and EAS group (grade 1: 2, grade 2: 4, grade3: 4, 1.31 ± 0.13) ($p=0.917$) (Table 1).

In EAS group, the mean ODI decreased after treatment. The pretreatment ODI was 38.3 ± 3.09 . At one month, the mean ODI was 35.60 ± 3.33 . In group EAC, the mean ODI decreased from 46.40 ± 3.97 before treatment to 43.08 ± 6.96 at one month after treatment ($p=0.174$) (Fig. 3). At

Three months after the procedure, 2 patients in the EAS group (20.0%) showed 'much improvement' in PGIC, 5 (50.0%) showed 'slight improvement' and 3 (30.0%) showed 'no improvement'. In the EAC group, 8 patients (38.1%) showed 'much improvement' in PGIC, 6 (28.6%) showed 'slight improvement' and 7 (33.3%) showed 'no improvement', which was not significantly different ($\chi^2=1.588$, $p=0.510$). In the EAS group, 1 patients increased their oral medication for pain control, 4 patients did not change their medication, 2 patients decreased oral medication, and 3 patients stopped medication. In the EAC group, one patient increased their oral medication for pain control, 13 patients did not change their medication, 3 patients decreased oral medication, and 4 patients stopped medication. These results were not significantly different

Table 1. Age, Symptoms, and Status of Lumbar Spine between EAS and EAC Groups

	EAS	EAC	p
Age	64.2 ± 3.5	66.19 ± 2.0	0.604
Duration of symptom	19.50 ± 5.6	15.25 ± 3.5	0.524
Initial ODI	38.3 ± 3.1	46.4 ± 4.0	0.212
Previous epidural injection	2.7 ± 0.7	4.5 ± 0.8	0.164
Previous lumbar surgery	1/10, 10.00%	9/21, 42.85%	0.106
Spinal stenosis grade	1.33 ± 0.20	1.31 ± 0.13	0.917

EAS: epidural adhesiolysis with single bolus injection, EAC: epidural adhesiolysis with continuous injection, ODI: Oswestry Disability Index.

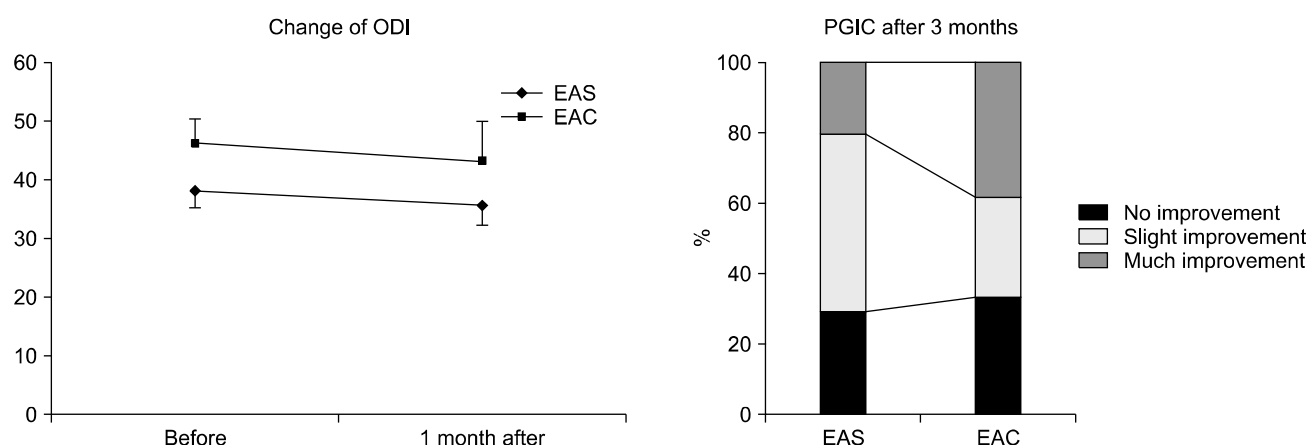


Fig. 3. Changes of ODI in EAS and EAC groups were presented and these changes were not significantly different one month after the procedure. Distribution of PGIC in EAS and EAC groups were not significantly different three months after the procedure. PGIC: Patient's Global Impression of Change, ODI: Oswestry Disability Index, EAS: epidural adhesiolysis with single bolus injection, EAC: epidural adhesiolysis with continuous injection.

Table 2. Age, Symptoms, and Status of Lumbar Spine between Responder and Non-responder Groups

	Responder	Non-responder	p
Age	67.5 ± 1.4	61.4 ± 4.3	0.208
Duration of symptom	17.8 ± 3.8	13.7 ± 4.6	0.522
Initial ODI	42.73 ± 3.96	46.17 ± 4.14	0.413
Previous epidural injection	3.7 ± 0.8	3.9 ± 0.8	0.853
Previous lumbar surgery	6/21 (28.6%)	4/10 (40.0%)	0.685
Spondylolisthesis	10/21 (47.6%)	4/10 (40.0%)	0.690
Foraminal stenosis	15/21 (71.4%)	8/10 (80.0%)	0.610

ODI: Oswestry Disability Index.

($\chi^2=1.378$, $p=0.775$).

Based on PGIC status, patients were categorized as non-responders (no improvement) or responders ('slight' or 'much improvement'). In the EAS group, 7 patients (70.0%, 95% confidence interval CI, 40.0%, 100.0%) were in responder group, 3 patients (30.0%, 95% confidence interval CI, 0%, 60.0%) were in non-responder group. In the EAC group, 14 patients (66.7%, 95% confidence interval CI, 47.6%, 85.7%) were in responder group, 7 patients (33.3%, 95% confidence interval CI, 14.3%, 57.1%) were in non-responder group. 10 patients were non-responders (5 men and 5 women) and 21 patients were responders (9 men and 12 women). The average age was 61.4 ± 4.3 years for non-responders and 67.5 ± 1.4 years for responders ($p=0.208$). The average duration of symptoms was 13.7 ± 4.6 months for non-responder group and 17.8 ± 3.8 months for responders ($p=0.522$). In responder group, the mean ODI decreased after treatment. The pretreatment ODI was 42.73 ± 3.96 . At one month, the mean ODI was 32.87 ± 4.96 . In non-responder group, the mean ODI increased from 46.17 ± 4.14 to 49.83 ± 6.75 at one month after treatment, which was significantly different ($p=0.008$).

The average number of previous epidural injections was 3.7 ± 0.84 for non-responders and 3.9 ± 0.85 for responders ($p=0.853$). four of 10 non-responders and 6 of 21 responders had previous lumbar surgery ($p=0.685$). The presence of spondylolisthesis or type of spinal stenosis (central or foraminal) did not differ statically between groups (Table 2).

One Patients treated with epidural adhesiolysis with indwelling catheter had transient urinary retention, but it resolved right after the epidural catheter was removed. During the procedure, the epidural catheter was partially

torn in two patients, but they had no abnormal signs for three months.

DISCUSSION

We found that epidural adhesiolysis with continuous infusion or a bolus injection improved clinical symptom in 70.0% and 66.7%, respectively, of patients who had previously shown poor improvement with an epidural steroid injection. However, continuous infusion was not superior to a bolus injection in terms of clinical symptoms, which suggests that epidural adhesiolysis might not washout inflammatory cytokines.

Considering that epidural adhesiolysis improved clinical symptoms in about 70% of patients refractory to conventional epidural steroid injection irrespective of continuous infusion or bolus injection, we postulate that accurate delivery of injected material to the lesion is most likely mechanisms for epidural adhesiolysis. A previous study suggested that limited effectiveness of conventional epidural injection may be because the injectate cannot spread to epidural adhesions properly.¹⁵ Likewise, Choi et al suggest that an inflatable balloon catheter may be an effective alternative to percutaneous epidural adhesiolysis when conventional methods fail to remove adhesions or sufficiently relieve stenosis because this is suitable for the targeted application of highly concentrated epidural medication.¹⁶

In this study, continuous infusion of a large volume was not superior to a bolus injection. These results differ from those of Rabinovitch et al, who reported that larger volumes of fluid injected in the epidural space resulted in greater relief of radicular leg pain and low back pain.¹⁰ The average volume used in Rabinovitch's study was 14.86 mL

(range: 2 to 42 mL), which was smaller than used in our study. However, they injected it as a single bolus injection rather than continuous infusion. Continuous infusion over 48 hours would allow the injectate to be absorbed, so volume might be more important for a bolus injection than for continuous infusion in spinal stenosis.

Unfortunately, we did not identify factors that affected clinical improvement of spinal stenosis in epidural adhesiolysis, although clinical symptoms improved in about 70% of cases. Age, sex, initial ODI, number of previous epidural injections, and duration of symptoms did not differ between non-responders and responders. Further studies to find factors that affect the improvement of spinal stenosis in epidural adhesiolysis are needed to popularize epidural adhesiolysis for managing spinal stenosis. Moon et al. demonstrated that a high intensity zone predicted a favorable long-term outcome after percutaneous epidural adhesiolysis for lumbar disc herniation.¹⁷ However, our patients had degenerative lumbar spinal stenosis, which did not have a high intensity zone. Lee et al. demonstrated that previous surgery, spondylolisthesis, and foraminal stenosis might be associated with poor prognosis in epidural adhesiolysis, which was not consistent with our study.¹⁸

This study has several limitations. One is the non-randomized study design. This non-randomized design might affect our results, but we mitigated possible biases caused by non-randomized design by recruiting patients sequentially with the same indication for treatment and restriction as indicated by Cox et al.¹⁹

There is also a limitation about the differences in the total amount of steroids used in the EAC and EAS groups. 20 mg of dexamethasone was used in the EAC group and 10 mg of dexamethasone was used in the EAS group. However, Waylon Wong et al reported a similar degree of analgesic efficacy in transforaminal epidural steroid injection using 3 mg of betamethasone and 6 mg of betamethasone, with no significant difference in reduction effect of NRS according to the total amount of betamethasone.²⁰ Also, Friedly et al reported that epidural injection of glucocorticoids plus lidocaine offered minimal or no short-term benefit as compared with epidural injection of lidocaine alone in spinal stenosis patient.²¹ Therefore, this study is designed assuming that the difference in analgesic effect with the amount of injected steroids is small, but the amount of drug was not controlled as a result.

The cost of a bolus injection and continuous infusion itself is not significantly different, but continuous infusion requires additional hospitalization for 3 days, resulting in additional costs. This cost difference might corroborate the results between groups. This study used PGIC and ODI to evaluate spinal stenosis. These were subjective and objective measures but adding measures such as claudication distance and a visual analog scale would have been better. The follow-up period was 3 months, which was short to evaluate spinal stenosis. Several studies on spinal stenosis have used 6 months to one-year follow-up, and further studies with long-term follow-up are needed.

CONCLUSIONS

Epidural adhesiolysis is a useful treatment for spinal stenosis considering that it improves clinical symptoms in more than half of spinal stenosis cases refractory to conventional epidural steroid injection. This result might be due to accurate delivery of medication, not a washout of inflammatory cytokines.

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