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Randomized Trial

Transforaminal vs Interlaminar Epidural Steroid Injection for Acute-Phase Shingles: A Randomized, Prospective Trial

Aki Fujiwara, MD, Keisuke Watanabe, MD, PhD, Keiji Hashizume, MD, PhD, Kozue Shinohara, MD, and Masahiko Kawaguchi, MD, PhD

From: Department of Anesthesiology Nara Medical University, Nara, Japan

Address Correspondence:
Aki Fujiwara, MD
Department of Anesthesiology
Nara Medical University
840 Shijo-cho, Kashihara,
Nara 634-8522, Japan
E-mail: higemo1117@yahoo.co.jp

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Background: The acute phase of shingles is characterized by severe pain, and one of the complications of shingles known as postherpetic neuralgia (PHN) is associated with prolonged pain. Although factors predicting the development of PHN, as well as its preventative measures, have been investigated, there is no single treatment effective for PHN. Some studies showed effectiveness of epidural injection to alleviate pain associated with acute-phase shingles. In these studies, epidural injection was performed by interlaminar (IL) approach. However, transforaminal (TF) approach may be more effective as it enables injection of steroids and local anesthetics closer to the dorsal root ganglion where inflammation primarily occurs. There have not been any studies comparing the analgesic effects of epidural injection approaches for pain associated with acute-phase shingles.

Objective: We compared the analgesic effects of IL and TF epidural injection approaches for pain associated with acute-phase shingles.

Study Design: We conducted a randomized prospective trial.

Setting: Nara Medical University Hospital, Department of Anesthesiology.

Methods: Forty patients with acute-phase shingles were randomly assigned to receive epidural steroid injections by TF or IL approaches. Patients were evaluated at the baseline, as well as at 1 month and 3 months after the treatment using the VAS and SF-36 scores. Patients with VAS score of over 40 at the 3-month follow-up were considered as having PHN, and the number of patients with PHN was compared between the IL and TF groups.

Results: Except the mental component of the SF-36 score and severity of skin rash, patient characteristics were not significantly different between the groups. VAS scores at 1 and 3-month follow-up were significantly lower than those at the baseline, and there was no difference between the groups. All SF-36 scores were not significantly different between groups at 1- and 3-month. There was no significant difference in the occurrence of PHN between the groups.

Limitations: We had a small sample size that did not reach the number of patients needed by the power analysis in the study. Then, our follow-up period of 3 months was relatively short.

Conclusions: VAS scores, the SF-36 RCS and MCS scores improved in both groups, however, there was no difference in the analgesic effects of the IL and TF epidural steroid injections at 1 and 3 months for acute-phase shingles patients.

Key words: Shingles epidural steroid injection interlaminar approach; transforaminal approach, fluoroscopic, postherpetic neuralgia, VAS, SF-36

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Shingles is a common disease, especially among the elderly population. The acute phase of shingles is characterized by severe pain, and one of the complications of shingles known as postherpetic neuralgia (PHN) is associated with prolonged pain (1,2). Although factors predicting the development of PHN (3-8), as well as its preventative measures, have been investigated, there is no single treatment effective for PHN. A randomized controlled trial (RCT) demonstrated that epidural steroid injection is effective to relieve pain associated with acute-phase shingles (9); however, the treatment is not preventative for PHN. A recent meta-analysis demonstrated that the early use of supplemental interventions, such as stellate ganglion block, paravertebral block (10), and epidural injection, are effective in reducing the occurrence of PHN (11).

Epidural steroid injection, when performed during the early onset of shingles, is theorized to reduce edema by suppressing the inflammation of nerve roots at an early stage. This will in turn facilitate healing of the affected nerves, suppressing progression to PHN and reducing the extent of pain.

In the previous RCT (9), epidural injection was performed by interlaminar (IL) approach. However, transforaminal (TF) approach may be more effective as it enables injection of steroids and local anesthetics closer to the dorsal root ganglion where inflammation primarily occurs. There have not been any studies comparing the analgesic effects of epidural injection approaches for pain associated with acute-phase shingles.

Thus, we performed a prospective RCT to compare the analgesic effects of IL and TF epidural injection approaches for pain associated with acute-phase shingles.

Objective

We performed epidural steroid injections via TF and IL approaches for pain associated with acute-phase shingles and compared the analgesic effects after one month. We further compared the extent of pain and the frequency of PHN occurrences 3 months after the treatment.

Methods

This randomized prospective study was conducted at Nara Medical University, Department of Anesthesiology. We determined sample size based on the assumption of Visual Analog Scale (VAS) score at one month: 30 in IL group, 15 in TF group, power of test 0.8, α= 0.05, SD = 20 . The sample size needed was 28 in each group. Institutional Review Board approval was obtained, and 40 consecutive patients with acute-phase shingles were enrolled in the study between June 2011 and October 2013. The diagnosis of shingles was made based on the clinical findings (unilateral painful skin rash with blisters along the dermatome) by dermatologists. Serological tests were not performed. All patients provided written or verbal consent.

Patients were included in the study if they were 60 years or older, presented to our clinic within 2 weeks from the initial onset of skin rash, had lesions appearing below level C6, and presented with initial VAS score of greater than 40 (patients rated their pain on a 100-mm line from no pain to unbearable pain).

Patients were excluded if they had the following conditions: reduced limb muscle strengths; bladder and bowel dysfunction; meningitis; disseminated zoster; kidney dysfunction (Cr > 1.5); unmanaged diabetes (HbA1c > 8.0); liver dysfunction (> Child B); gastrointestinal ulcers; allergy to contrast agents, local anesthetics, steroids, or analgesics; and infections at the site of injection. Patients were also excluded if they were on anticoagulants or anti-platelet agents and were unable to withhold from these medications.

At initial presentation, patients were stratified based on their age and gender, and were randomly assigned to receive epidural steroid injections by TF or IL approaches using the block randomization system. There were 4 pain management specialists in our institution. All 4 specialists performed interventions and follow-up visits for their own patients. The specialist who performed the intervention evaluated the patient during the follow-up visits. Both the patients and the experts were not blinded because of the nature of the intervention. Experts from our pain clinic examined the patients, and the dermatome map of the body was used to determine the level of affected nerve root from the location of skin rash. Skin rash was considered severe if it involved 80% or more of the dermatome, moderate if it involved 30-79% of the dermatome, and mild if it involved less than 30% of the dermatome.

Patients' Evaluation

Patients were evaluated at the baseline, as well as at one month and 3 months after the treatment using the VAS and 36-Item Short Form Health Survey (SF-36) scores. VAS score, in which patients rated their pain on a 100-mm line from no pain to unbearable pain (left to right), was used to evaluate the extent of pain, and SF-36 was used to evaluate health-related quality of life. SF-36 consists of 8 scaled scores (vitality, physical

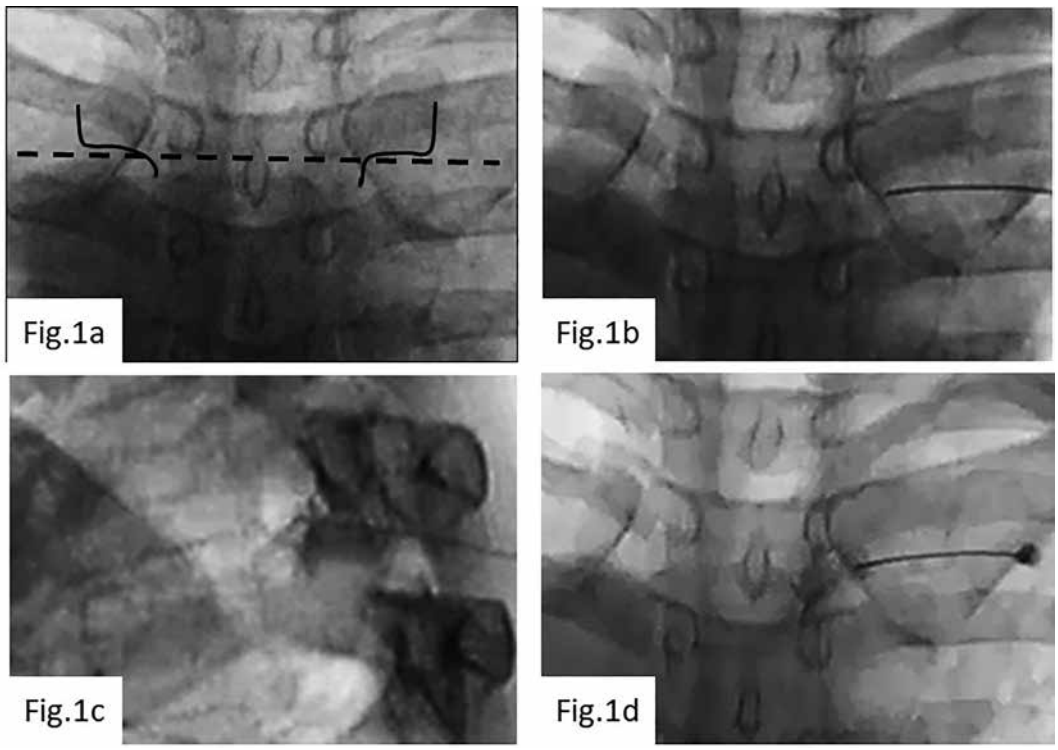

Fig. 1. *Illustration of transforaminal approach A. The padicle of vertebral arch was aligned with the lower edge of transverse process. B. The needle tip reached to the base of the transverse process C. The needle was slid under the transverse process into the intervertebral foramen (lateral view) D. Anteroposterior view.*

functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, and mental health), which are the weighted sums of the questions in each section. Each scale is directly transformed into a 0-100 scale on the assumption that each question carries equal weight. The lower the score the more disability. The higher the score the less disability.

Patients with VAS score of over 40 at the 3-month follow-up were considered as having PHN, and the number of patients with PHN was compared between the IL and TF groups.

Interventions

Both injections were performed within 3 days of the initial presentation, and again after one week in both groups.

Epidural puncture was performed close to the affected level. For example, when the left nerve root was affected at T4, injections were performed at T4/5 in the IL group and at left T4 in the TF group. Both IL and TF injections were performed by experienced physicians in the pain clinic under real-time fluoroscopic guidance.

TF group: Patients were placed in a prone position on an x-ray table, and their skin surface was disinfected. The fluoroscopy angle was adjusted so that the pedicle of vertebral arch was aligned with the lower edge of the transverse process (Fig. 1a). Using a 25-gauge, 60 mm Cattelan needle (Quincke needle, Hakko), a puncture was performed at the point of 4 cm away from the spinous process along the alignment. The needle tip reached to the base of the transverse process (Fig. 1b); then the needle was slid under the transverse process into the intervertebral foramen (Fig. 1c, 1d). One milliliter of Iohexol was used to confirm the appropriate placement of the needle, and 1.65 mg dexamethasone and 1 mL of 2% mepivacaine hydrochloride were injected (Fig. 2a, 2b).

IL group: Patients were placed in a prone position on an x-ray table, and their skin surface was disinfected. The fluoroscopy angle was adjusted so that the space between the vertebral arch where injection was planned

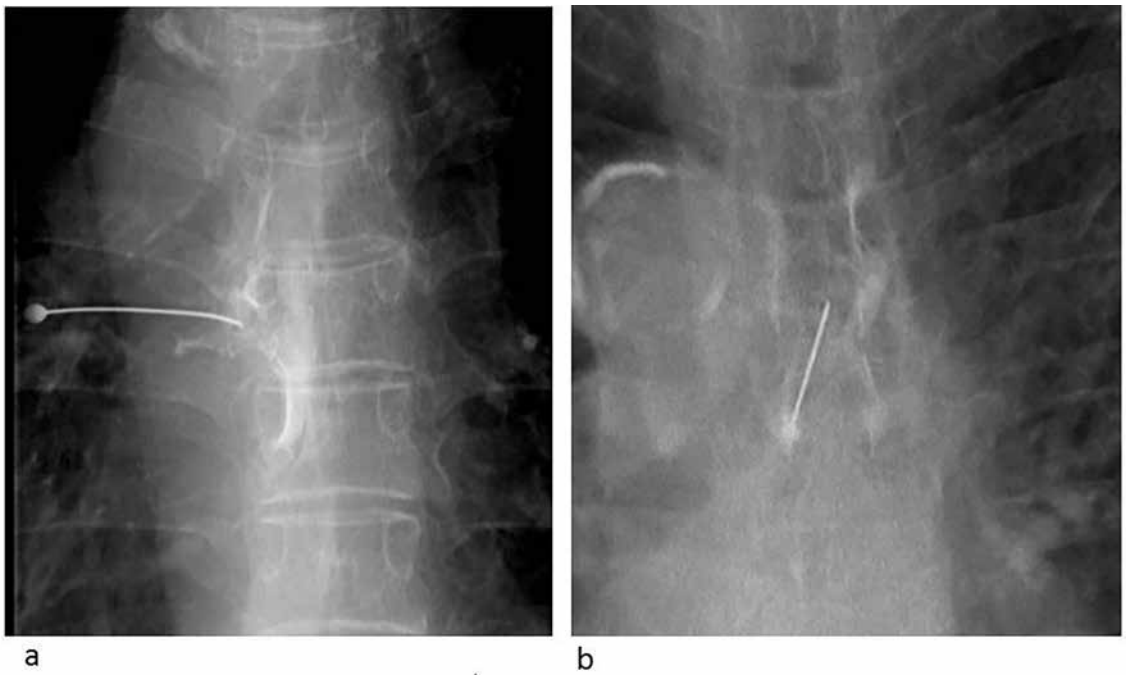

Fig. 2. *Fluoroscopic images. A. Transforaminal approach. B. Interlaminar approach.*

was widely visible. One percent mepivacaine was injected to induce local anesthesia, and a 22-gauge, 60 mm block needle (Quincke needle, Hakko) was inserted from the same injection site. X-ray fluoroscopy was used to visualize the block needle, and the loss of resistance technique was used with saline to reach into the epidural space. One milliliter of Iohexol was used to confirm the appropriate placement of the needle tip into the epidural space, and 1.65 mg dexamethasone and 4 mL of 0.5% mepivacaine hydrochloride were injected.

Following both injections, patients rested in bed for 45 minutes and their blood pressure, heart rate, and arterial oxygen saturation were monitored. After the 45-minute rest, patients were discharged after confirming the absence of any complications due to the treatment.

Medication

All patients had been prescribed antiviral drugs (valaciclovir or famciclovir) at the time of initial presentation to our clinic.

All patients were prescribed 60 mg loxoprofen three times a day to manage their pain. In addition, patients were prescribed 0.5 mg etizolam to take before sleep if they presented with insomnia due to the pain. Patients were also prescribed with a dose of codeine phosphate (20 mg/dose) if they had unbearable pain within one month after the onset of shingles. Administration of other medications, such as anti-depressants, anti-epileptic agents, opioids, and anti-anxiety drugs other than etizolam were prohibited within the one-month period. These drugs were prescribed after one month when appropriate, as determined by the physician in charge.

Statistical Analysis

Statistical analyses were performed to compare the data between the 2 groups. T-tests were used to compare age, gender, BMI, time from the appearance of skin rash to the initial presentation to our clinic, the initial VAS score, and the initial SF-36 score. Chi-square tests were used to compare the location of the affected area (the thoracic vertebrae or lumbar vertebrae), the presence of allodynia, and the rate of PHN occurrences. Mann-Whitney U tests were used to compare the extent of the loss of sensation in the skin and the severity of skin rash. Two-factor factorial ANOVA was used to compare the VAS and SF-36 scores at the baseline, 1-month, and 3-month follow-up. A *P* value of less than 0.05 was considered significant.

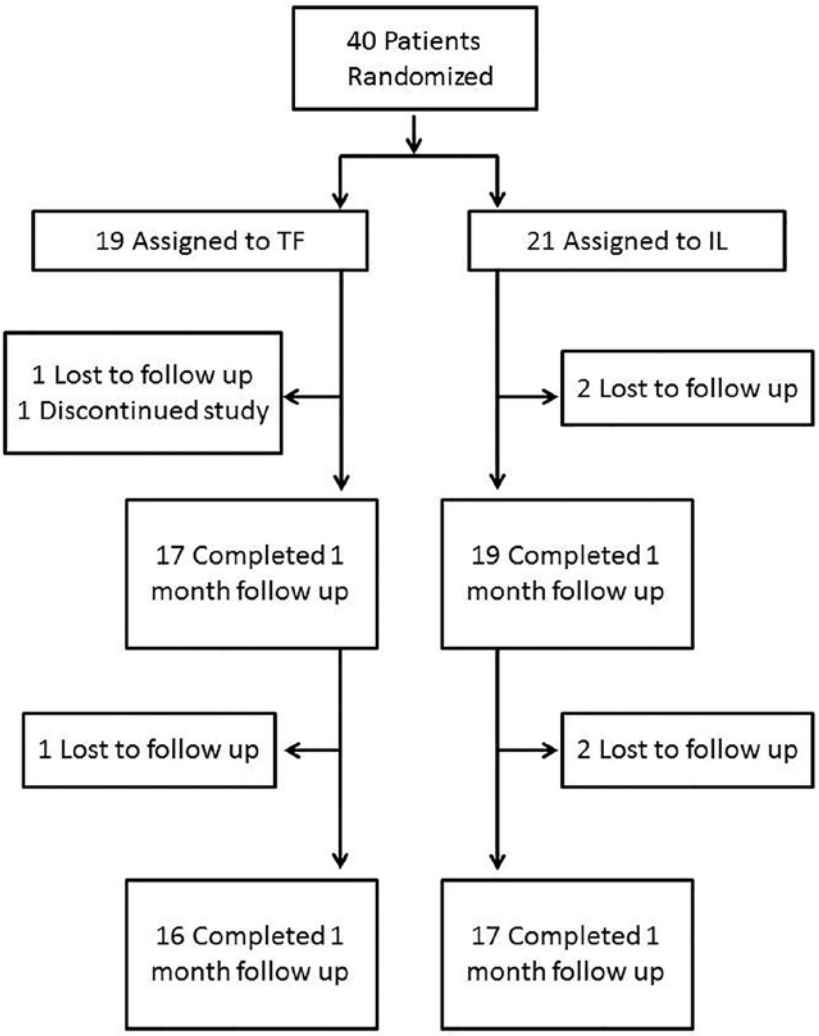

Fig. 3. *Flow chart of patient enrollment*

Results

A total of 40 patients were randomly assigned to receive injections either by TF approach (n = 19) or IL approach (n = 21). In the TF group, one patient was lost to follow-up at the time of the first treatment, and one patient discontinued the study between the first and second treatments since advanced treatments, such as thoracic sympathetic ganglion block and spinal cord stimulation, were required due to the progressive decrease of muscle strength in the upper limbs. In the IL group, 2 patients were lost to follow-up at the time of the first treatment. At one month following the treatment, 17 patients in the TF group and 19 patients in the IL group were evaluated.

After the 1-month follow-up, an additional one patient in the TF group and 2 patients in the IL group were lost to follow-up. At the 3-month follow-up, 16 patients in the TF group and 17 patients in the IL group were evaluated (Fig. 3).

Patient characteristics are summarized in Table 1. Age, gender, and BMI of the patients were not significantly different between the groups. Similarly, there were no significant differences between the groups in terms of the initial VAS score, the lesion level, the time

Table 1. *Demographic data*.

	TF	IL	*P* value
Age	71 ± 7.7	71 ± 5.6	0.73
Gender (Men:Women)	7 : 10	8 : 11	0.95
BMI (Body Mass Index)	22.1 ± 3.25	21.9 ± 3.64	0.86
Lesion Level (Thoracic: Lumbar)	14 : 3	13 : 6	0.33
Period (Days) (Rash Onset:Intervention)	8.65 ± 4.25	3.81 ± 4.46	0.81
Sensory (Normal:Hypesthesia:Hypersethesia:Loss)	4 : 8 : 3 : 2	3 : 6 : 9 : 1	0.30
Allodynia (Yes:No)	10: 7	13 : 6	0.55
Rash Severity (Severe:Moderate:Trivial)	1 : 5 : 11	9 : 4 : 6	0.019
Primary VAS	75.6 ± 13.8	65.3 ± 18.2	0.07
Primary SF36			
PCS (Physical Health)	40.3 ± 17.4	36.1 ± 15.5	0.49
MCS (Mental Health)	38.8 ± 11.4	47.5 ± 10.2	0.033
RCS (Social Health)	46.8 ± 9.48	48.5 ± 8.61	0.78

Baseline demographic and clinical characteristics for each group
Values are mean ± SD or number of patients.
Except severity of skin rash and the mental component of the SF-36 score, patients' characteristics were not significantly different between groups.
Skin rash was considered severe if it involved 80% or more of the dermatome, moderate if it involved 30-79%, and mild if it involved less than 30%.
TF: Transforaminal approach, IL: Interlaminar approach
VAS: Visual Analog Scale, SF-36: 36-Item Short Form Health Survey

period from the onset of rash to the first intervention with nerve blocks, the degree of sensory loss, and the presence of allodynia. There were no significant differences in the physical component (PCS, physical health) and the role component (RCS, role/social health) of the SF-36 score at baseline; however, the mental component (MCS, mental health) of the SF-36 score was significantly lower in the TF group compared with the IF group (P = 0.033). Patients in the IL group also had more severe forms of skin rash (P = 0.019) than those in the TF group. There were no patients who took any analgesics at baseline.

There were no complications associated with technical procedures, such as puncture of the dura, damage to the nerves, bleeding, and infections. There were no side effects associated with the medications, including allergic reactions.

The initial VAS score was 75.6 ± 13.8 and 65.3 ± 18.2 (mean ± SD) in the TF and IF groups, respectively, and the difference was not statistically significant. There was a statistical interaction between the approaches and time. VAS scores at 1- and 3-month follow-up were significantly lower than those at baseline (P = 2.6×10-20), and there was no difference between the groups (P = 0.56) (Fig. 4).

There were no significant differences in the SF-36 PCS (physical health) scores at baseline, 1- and 3-month follow-up, and the differences between the treatment groups were not significantly different at each time point (Fig. 5a).

SF-36 MCS (mental health) scores were significantly lower in the TF group at baseline (P = 0.033). There was a significant improvement in the MCS score for both groups at 1- and 3-month follow-up from baseline (P = 0.0013), and there was no significant difference between the groups (P = 0.25) (Fig. 5b).

SF-36 RCS (role/social health) significantly improved for both groups at 1- and 3-month follow-up from baseline (P = 0.0019), and there was no significant difference between the groups (P = 0.55) (Fig. 5c).

There was no significant difference between the groups in the occurrence of PHN, calculated as the proportion of patients with VAS scores greater than 40 at the 3-month follow-up (P = 0.10).

Discussion

To date, the efficacy of nerve block treatment for pain associated with shingles has been evaluated in a limited number of prospective RCTs. They include studies on epidural steroid injections, stellate ganglion block, and paravertebral block for pain associated with acute-phase shingles. Makharita et al performed a

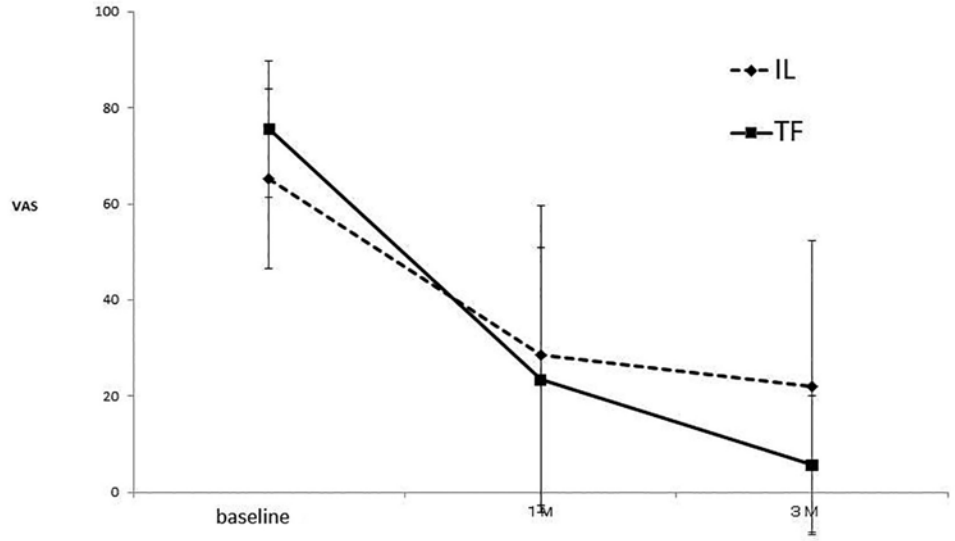

Fig. 4. *Changes in VAS (Visual Analog Scale) after procedure. VAS scores at 1 and 3-month follow-up were significantly lower than those at baseline, and there was no difference between the groups.*
IL: Interlaminar approach, TF: Transforaminal approach

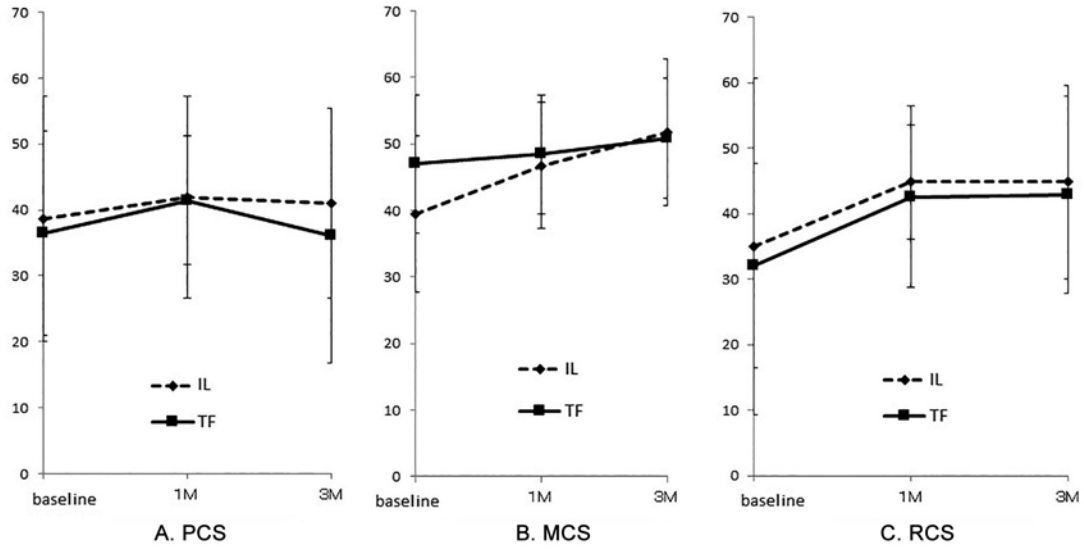

Fig. 5. Mean SF-36 score before and after procedure. SF-36 indicates quality of life measure with no significant difference between groups at 1 and 3 months. A. SF-36 PCS (physical health) scores. B. SF-36 MCS (mental health) scores. C.SF-36 RCS (role/social health) scores.

double-blind RCT to compare the efficacy of paravertebral blocks with placebo for acute-phase shingles in 143 patients over 50 years of age (10). They demonstrated that the active group had a significantly shorter time to pain resolution and healing of the skin rash, as well as lower incidence of PHN after 6 months.

One of the studies on epidural steroid injection evaluated the short-term analgesic effect of a single epidural steroid injection (9). In this study, 598 patients with acute-phase shingles were randomly assigned to receive either a standard therapy (group A) or a standard therapy + one additional epidural steroid injection (group B) to evaluate their VAS scores at 1, 3, and 6 months after the treatment. The VAS score was significantly lower in group B at 1 month, although there was no significant difference between the groups at 3 months after the treatment.

Pasqualucci et al (12) randomly assigned 569 patients with acute-phase shingles to receive either intravenous anti-virus agent plus 60 mg prednisolone (group A), or epidural injection of 40 mg methylprednisolone and local anesthetic by placement of epidural catheter under fluoroscopic guidance (group B). Treatments were administered for one week in both groups. Complete recovery, defined as the proportion of patients without pain or abnormal sensations, at 1, 3, 6, and 12 months after the treatment was significantly higher in group B, suggesting that the epidural administration of steroids and local anesthetics may be more effective than intravenous administration to prevent the development of PHN.

A recent meta-analysis demonstrated that early supplemental interventions reduce the occurrence of PHN (11), indicating that epidural steroid injection may be an effective method to prevent PHN.

Epidural steroid dosing in our study (1.65 mg dexamethasone) is lower than that in the above-mentioned studies (9,12). There is a randomized double-blind trial which examined the effective dose of steroids in TFESI for pain reduction in patients with lumbosacral radiculopathy (13). In this study, 160 patients were randomly assigned to four groups (epidural injections of either 5 mg, 10 mg, 20 mg, or 40 mg of triamcinolone). All groups showed improvement in the verbal numerical rating scale at one week after the second TFESI. However, the group treated with 5 mg triamcinolone showed less improvement in the degree of participant satisfaction compared to the other groups. They concluded that the dose of at least 10 mg triamcinolone is sufficient to provide significant pain relief. Particulate steroids such as triamcinolone have a potential risk of spinal cord infarction due to embolism of radicular vessels. Thus we always use 1.65 mg dexamethasone, which has an equivalent strength to 10 mg triamcinolone for epidural injections in order to avoid potential adverse effects from an excess of exogenous corticosteroids.

Epidural steroid injections can be performed by TF or IL approaches. A study suggested that the TF approach is more effective than other methods for the treatment of lumbar radiculopathy (14). In addition, since only 36% of the injected volume spreads into the ventral epidural space by the IL approach (15), the TF approach may be more appropriate for patients in which radiculitis, which can be caused by herniated disks, is the primary cause of pain (16-18). The proposed benefit of the transforaminal approach is to place higher concentrations of corticosteroid and anesthetic preparations close to the nerve root/disc interface (15). Furthermore, a study demonstrated that the TF approach results in fewer severe complications, such as direct damage to the spinal cord and spinal cord compression by hematoma (19).

There have not been any studies that compared the analgesic effects of different epidural steroid injection approaches for acute zoster-associated pain. We expected that the TF approach may be more effective as it enables injection of steroids closer to the dorsal root ganglion where inflammation primarily occurs. Although our findings did not demonstrate any difference between the 2 approaches in terms of the efficacy of the treatment, the VAS score was significantly lower at 1 and 3 months following the treatment in both groups. This suggests that epidural steroid injection is effective in managing pain for patients with acute-phase shingles, although pain may have been reduced spontaneously in some patients given its acute nature.

Our findings may be explained by the higher injection volume (mL) in the IL group compared with the TF group. Given the same amount (mg) of the local anesthetic for both groups, a total of 4.5 mL was injected by the IL approach, and 1.5 mL was injected by the TF approach. This difference in the injection volume may have caused the difference in the washout effect of inflammatory substances. In a RCT comparing the effects of the volume of local anesthetic in epidural TF injection for patients with lumbar radiculopathy, a significantly higher proportion of patients in the high-volume group reported reduced VAS scores at 4 weeks after the treatment (20). This finding suggests that high-volume injection of local anesthetics has several effects, including dilution of inflammatory cytokines, removal of adhesions, improvement of blood circulation, suppression of ectopic discharge of affected nerves, and reduction of central sensitization. Therefore, our findings may have been different if the injection volume (mL) had been kept consistent between the groups.

Both TF and IL approaches have merit and demerit. We consider that the TF approach has 5 advantages and 4 disadvantages. First, the TF approach is less likely to cause direct damage to the spinal cord. Second, it has a lower mass effect on the spinal canal when bleeding occurs. Third, it can be performed postoperatively for patients who have undergone surgical procedures such as laminectomy. Fourth, it is less technically challenging, especially for injections into the mid-thoracic vertebrae. Lastly, it allows injection of drugs only into the side of the lesion. In fact, a study compared the spread of a drug by fluoroscopy and demonstrated that the drug spread into the ventral epidural space more effectively and was less likely to spread into the opposite side when injected by the TF approach compared to the IL approach (21). Thus, the TF approach may lower the risk of side effects associated with the spread of drugs to the healthy side, such as reduced blood pressure and transient reduction of muscular strength in the lower limbs.

Disadvantages of the TF approach include the need for an x-ray fluoroscopy system. In addition, the TF approach has potential risk of inadvertent puncture of the pleura, and in rare cases, can infarct the spinal cord by injuring or embolizing the radicular vessels (22). Furthermore, there is the risk of damage to the nerve roots.

In the present study, our findings may have been different if intraneural injection had been performed. However, we did not consider intraneural injection as an option as it is associated with strong pain and may cause additional damage to the nerves.

The SF-36 MCS (mental health) score was significantly lower in the TF group at baseline; however, it improved after 1 month to a point where there was no significant difference in SF-36 scores between the 2 groups. The results demonstrated that the efficacy of the TF approach with respect to analgesic impact, is equivalent to that of the IL approach. Reduction of VAS scores at 1 and 3 months after the treatment was associated with a significant improvement in SF-36 MCS (mental health) and RCS (role/social health) scores, suggesting that pain may be correlated with health-related quality of life.

There are 2 limitations to the present study. First, we had a small sample size in the study. There were only 40 patients who satisfied our inclusion criteria during our study period. Given that there was no statistically significant difference between the groups at the end of our study period, we did not prolong the study to include more patients.

Second, our follow-up period of 3 months was relatively short. However, patients with prolonged pain required additional treatments, such as sympathetic ganglion block and spinal cord stimulation, to relieve the pain. We considered it unethical to continue the study for all patients with the same condition without providing additional treatments to those who needed them.

Conclusion

Analgesic effects were observed and the SF-36 RCS (role/social health) and MCS (mental health) scores improved when injections were performed by both approaches; however, there were no differences in the analgesic effects of the IL and TF epidural steroid injections at 1 and 3 months for acute-phase shingles patients.

References

1. Johnson RW, Alvarez-Pasquin MJ, Bijl M, Franco E, Gaillat J, Clara JG, Labetoulle M, Michel JP, Naldi L, Sanmarti LS, Weinke T. Herpes zoster epidemiology, management, and disease and economic burden in Europe: A multidisciplinary perspective. *Therapeutic Advances Vaccines* 2015; 3:109-120.
2. Bricout H, Perinetti E, Machettini P, Ragni P, Zotti CM, Gabutti G, Volpi A, Franco E. Burden of herpes zoster-associated chronic pain in Italian patients aged 50 years and over (2009-2010): A GP-based prospective cohort study. *BMC Infectious Diseases* 2014; 14:637.
3. Opstelten W, Zuithoff NPA, van Essen GA, Loon AM, van Wijck AJM, Kalkman CJ, Verheij TJM, Moons KGM. Predicting postherpetic neuralgia in elderly primary care patients with herpes zoster: Prospective prognostic study. *Pain* 2007; 132:S52-S59.
4. Oxman MN, Levin MJ, Johnson GR, Schmader KE, Straus SE, Gelb LD, Arbeit RD, Simberkoff MS, Gershon AA, Davis LE, Weinberg A, Boaedman KD, Williams HM, Zhang JH, Peduzzi PN, Beisel CE, Morrison VA, Guatelli JC, Brooks PA, Kauffman CA, Pachucki CT, Neuzil KM, Betts RF, Wright PF, Griffin MR, Brunell P, Soto NE, Marques AR, Keay SK, Goodman RP, Cotton DJ, Gnann JW, Loutit J, Holodniy M, Keitel WA, Crawford GE, Yeh SS, Lobo Z, Toney JF, Greenberg RNm Keller PM, Harbecke R, Hayward AR, Irwin MR, Kyriakides TC, Chan CY, Chan ISF, Wand WWB, Annunziato PW, Silber JL. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med* 2005; 352:2271-2284.
5. Lal H, Cunningham AL, Godeaux O, Chlibek R, Diez-Domingo J, Hwang SJ, Levin MJ, McElhaney JE, Poder A, Puig-Barbera J, Vesikari T, Watanabe D, Weckx L, Zahaf T, Heineman TC. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. *N Engl J Med* 2015; 372:2087-2096.
6. Kawai K, Rampakakis E, Tsai TF, Cheong HJ, Dhitavat J, Covarrubias AO, Yang L, Cashat-Cruz M, Monsanto H, Johnson K, Sampalis JS, Acosta CJ. Predictors of postherpetic neuralgia in patients with herpes zoster: A pooled analysis of prospective cohort studies from North and Latin America and Asia. *International Journal of Infectious Disease* 2015; 34:126-131
7. Bouhassira D, Chassany O, Gaillat J, Hanslik T, Launay O, Mann C, Rabaud C, Rogeaux O, Strady C. Patient perspective on herpes zoster and its complications: An observational prospective study in patients aged over 50 years in general practice. *Pain* 2012; 153:342-349.
8. Wu CL, Marsh A, Dworin RH. The role of sympathetic nerve blocks in herpes zoster and postherpetic neuralgia. *Pain* 2000; 87:121-129
9. van Wijck AJM, Opstelten W, Moons KGM, van Essen GA, Stolker RJ, Kalkman CJ, Verhij TJM. The PINE study of epidural steroids and local anaesthetics to prevent postherpetic neuralgia: A randomized controlled trial. *Lancet* 2006; 367:219-224.
10. Makharita MY, Amr YM, El-Bayoumy Y. Single paravertebral injection for acute thoracic herpes zoster: A randomized controlled trial. *Pain Practice* 2015; 15: 229-235
11. Xing XF, Zhou ZF, Zhang FJ, Yan M. The effect of early use of supplemental therapy on preventing postherpetic neuralgia: A systematic review and meta-analysis. *Pain Physician* 2017; 20:471-486.
12. Pasqualucci A, Pasqualucci V, Galla F, de Angelis V, Marzocchi V, Colussi R, Paoletti F, Girardis M, Lugano M, del Sindaco F. Prevention of post-herpetic neuralgia: Acyclovir and prednisolone versus epidural local anesthetic and methylpredonisolone. *Acta Anesthesiol Scand* 2000; 44:910-918.
13. Kang SS, Hwang BM, Son HJ, Cheong IY, Lee SJ, Lee SH, Chung TY. The dosages of corticosteroid in transforaminal epidural injections for lumbar radicular pain due to a herniated disc. *Pain Physician* 2011; 14:361-370.
14. Plastaras C, McCormick ZL, Garvan C, Macron D, Joshi A, Chimes G, Smeal W, Rittenberg J, Kennedy DJ. Adverse events associated with fluoroscopically guided lumbosacral transforaminal epidural injections. *Spine J* 2015; 15:2157-2165.
15. Botwin KP, Natalicchio J, Hanna A. A fluoroscopic guided lumbar interlaminar epidural injections: A prospective evaluation of epidurography contrast patterns and anatomical review of the epidural space. *Pain Physician* 2004; 7:77-80.
16. Cohen SP, Bicket MC, Jamison D, Wilkinson I, Rathmell JP. Epidural steroids: A comprehensive, evidence-based review. *Reg Anesth Pain Med* 2013; 38:175-200.
17. Riew KD, Yin Y, Gilula L. The effect of nerve root injections on the need for operative treatment of radicular pain: A prospective, randomized, controlled double blind study. *J Bone Joint Surg* 2008; 82A:1589-1593.
18. Karppinen J, Malmivaara A, Kurunlchti M. Periradicular infiltration for sciatica: A randomized controlled trial. *Spine* 2001; 26:1059-1067.
19. McGrath JM, Schaefer MP, Malkamaki DM. Incidence and characteristics of complications from epidural steroid injections. *Pain Medicine* 2011; 12:726-731.
20. Chun EH, Park HS. Effect of high-volume injectate in lumbar transforaminal epidural steroid injections: A randomized, active control trial. *Pain Physician* 2015; 18:519-525.
21. Botwin K, Natalicchio J, Brown LA. Epidurography contrast pattern with fluoroscopic guided lumbar transforaminal epidural injections: A prospective evaluation. *Pain Physician* 2004; 7:211-215.
22. Nahm FS, Lee CJ, Lee SH, Kim TH, Sim WS, Cho HS, Park SY, Kim YC, Lee SC. Risk of intravascular injection in transforaminal epidural injections. *Anesthesia* 2010; 65:917-921.