Retrospective Study

# Transforaminal Epidural Steroid Injection for Zoster-Related Pain: The Golden Period for the Best Outcome

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Disclaimer: This work was supported by a research grant of Seoul National University Bundang Hospital (11-2012-014).

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 11-18-2020 Revised manuscript received: 11-23-2020 Accepted for publication: 01-20-2021

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**Background:** Zoster-related pain (ZRP) has many negative effects on a patient's quality of life. The transforaminal steroid injection (TFESI), which reduces neural inflammation and pain, has been advocated by pain physicians. Many reports demonstrated that early administration of TFESI showed better efficacy; however, the golden period during which TFESI is most effective remains unclear.

**Objectives:** This multicentre retrospective cohort study aimed to identify the golden period by which TFESI yields the best outcome in patients with ZRP.

**Study Design:** Multicenter, retrospective cohort study.

**Setting:** University-affiliated hospitals.

**Methods:** After performing the TFESI in patients with ZRP, the patients were classified into two groups: the effective group (E) and the not effective group (N) based on the changes in the pain intensity 3 months after the TFESI. The receiver operating characteristic (ROC) curve analysis was used to assess the cut-off time point for predicting TFESI effectiveness. Furthermore, a logistic regression analysis was performed to identify patients' factors associated with a successful treatment outcome.

**Result:** Of the 302 patients, 186 and 116 patients were classified into the E and N group, respectively. ROC curve analysis showed that the best cut-off time point for TFESI was 12 weeks (95% confidence interval [CI]; 10-14 weeks) after the onset of HZ. The only variable associated with a favorable outcome was a symptom duration of ≤ 12 weeks compared with > 12 weeks (Odd ratio, 0.107; 95% CI, 0.055-0.205; $P < 0.001$). Other patient variables were not significantly associated with the effectiveness of TFESI. TFESI was most effective when administered within 12 weeks of the onset of herpes zoster.

**Limitation:** This study was not a prospective randomized controlled trial (RCT) and the follow-up period was only 3 months after TFESI.

**Conclusion:** TFESI is more effective when administered within 12 weeks of onset of herpes zoster.

**Key words:** Herpes zoster, injections, epidural, nerve block, neuralgia, pain management, ROC curve, therapeutics, treatment outcome, regression analysis

**Institutional Review Board (IRB) approval:** This multicenter, retrospective cohort study was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (IRB no. B-1910-570-101).

**Pain Physician 2021: 24:E669-E676**

Zoster-related pain (ZRP) is one of the most frequent causes of neuropathic pain and occurs after herpes zoster (HZ) infection (1,2). The burden of ZRP can have an enormous negative impact on the quality of life of patients. ZRP is caused by inflammation of the dorsal root ganglia (DRG) of the spinal nerves and sensitization of the peripheral nervous system (3). The latent varicella-zoster virus (VZV) is located in the DRG after primary infection, and reactivation of the virus results in skin lesions and peripheral nerve inflammation (4). Furthermore, hypoxic damage, neuronal loss, or injuries in the DRG may persist for months, and further sensitization of the central nervous system may occur (5). This pathophysiology causes intractable pain in the affected dermatome.

Epidural steroid injection (ESI) has been used for treating ZRP in the acute phase of HZ by reducing neuronal inflammation in the affected spinal nerves. A randomized controlled trial showed that a single ESI administered in the acute phase of HZ had a significant pain-relieving effect for approximately one month (6). However, there has been controversy as to whether this procedure can reduce the incidence of postherpetic neuralgia (PHN) caused by HZ (6-8). Moreover, the transforaminal epidural steroid injection (TFESI) has been advocated over a simple ESI for reducing pain in patients with ZRP (9) because TFESI has the advantage of delivering medications directly to the target spinal nerve root and DRG. TFESI targets the neural structures in the anterior epidural space, including the adjacent neural tissue and DRG, which are considered to be important for the treatment of ZRP.

There have been many reports on the treatment effectiveness of TFESI on PHN (10-12). Earlier administration of TFESI can increase the possibility of complete relief from PHN (13). Furthermore, anecdotal experience at our institute suggested that delayed administration of TFESI had a poor effect on reducing ZRP. Nevertheless, there have been no studies regarding the golden period for which TFESI can show good treatment effect. In addition, little information is available on patient factors that are associated with the effectiveness of TFESI in patients with ZRP.

In these regards, the primary purpose of this study was to identify the time point or golden period by which TFESI should be performed to achieve the most effective pain reduction, and secondly to identify any predictive factors that may affect pain reduction resulting from TFESI in patients with ZRP.

## Methods

### Patients

This multicenter, retrospective cohort study was conducted in 3 university-affiliated hospitals in South Korea. This study was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (IRB no. B-1910-570-101). After obtaining approval from the IRB, the medical records of consecutive patients who underwent TFESI between January 2014 and December 2017 at 3 university hospital were reviewed.

Inclusion criteria were as follows: patients (1) with ZRP in a single dermatome in the thoracic and lumbar region; (2) with a history of receiving antiviral medications; (3) with a history of receiving TFESI for ZRP; and (4) whose 3-month follow-up data after TFESIs were available. Exclusion criteria were as follows: patients (1) with affected region above the T1 dermatome; and (2) whose 3-month follow-up data after TFESIs were unavailable.

### TFESI Procedure

All TFESIs were performed under fluoroscopic guidance. The patient was laid down on a radiologic table in prone position and vital signs (blood pressure, pulse oximetry, electrocardiogram) were monitored. After aseptic draping of the overlying skin, the fluoroscopic beam was aligned to an ipsilateral 20-25° oblique angle. The skin entry point was marked just inferior and lateral to the pedicle, and skin infiltration with 1% lidocaine was performed for local anaesthesia. A Quincke type, 22-gauge, 12-cm spinal needle (Taechang Industrial Co., Kongju, Korea) was advanced towards the target point using the tunnel vision technique to the posterior margin of the vertebral body under fluoroscopic guidance. When the tip of the needle was positioned at the correct location, 1-2 mL of contrast agent (Omnipaque®; Nycomed Ireland, Ltd., Cork, Ireland) was injected to confirm epidural spread and to identify any intravascular or intrathecal spread. After the proper positioning of the needle was confirmed, 3 mL of 0.18% ropivacaine with 5 mg of dexamethasone was injected. Following the injection, the patient was monitored closely in the recovery room for any signs of complications.

### Outcome Measurement

At their first visit, the following data for each patient were obtained: age, gender, height, weight, symptom duration before the TFESI, dermatome of the

affected site, initial pain intensity measured by 10-cm visual analog scale (VAS, 0 = no pain; 10 = the worst pain imaginable), number of TFESIs, current medication (use of strong opioid analgesics, including oxycodone, hydromorphone, morphine, and transdermal fentanyl; non-opioid analgesics, including tramadol, nonsteroidal anti-inflammatory drugs (NSAIDs), and acetaminophen; anticonvulsants, including pregabalin and gabapentin; and antidepressants), and comorbidities such as diabetes mellitus (DM) and cancer.

At follow up visits (2 weeks, 2 months, and 3 months) after the final TFESI, the average daily pain intensity (VAS scores) and 5-point patient satisfaction scale (1 = significantly aggravated; 2 = slightly aggravated; 3 = no change; 4 = slightly improved; 5 = significantly improved) scores were recorded.

### Statistical Analysis

The patients were categorized into 2 groups, 3 months after the TFESI: the effective (E) group or the not effective (N) group based on the VAS score. Patients in the E group were defined as having a 50% or more reduction in the VAS score, and the remaining patients were categorized in the N group.

After categorization, receiver operation characteristic (ROC) curve analysis was performed to determine the cut-off time point for the TFESI golden period. The cut-off value was calculated from the maximum value of Yoden's J statistics. The 95% confidence interval (CI) for cut-off time point was calculated with a bootstrapping method (2000 iterations with 300 random number seed). Also, logistic regression was performed to calculate the adjusted odds ratio (OR) with a 95% confidence interval (CI) to identify patient factors associated with a successful TFESI. Hosmer-Lemeshow goodness of fit was used to test the estimated logistic regression model. The required sample size was calculated under the following conditions with G*power software version 3.1.9.6 (Heinrich-Heine-Universität Düsseldorf, Germany), as reported previously (14, 15): (1) the primary independent variable (X) was symptom duration, and the primary outcome (Y) was the effect of TFESI; (2) expected OR = 0.1; (3) $R^2$ other X = 0; (4) probability (Y = 1|X = 1) under the null hypothesis = 0.1; (5) binominal distribution of X (≤ 12 weeks vs > 12 weeks) with a probability of 0.5; and (6) $\alpha$ = 0.05 and power (1 - $\beta$) = 0.9 for 1-tailed test. The period of 12 weeks was chosen from the result of the ROC curve analysis. This estimation yielded a sample size of 247 patients. Continuous and categorical variables in each group were tested using student t test and chi-square test, respectively. Statistical software SPSS version 22.0 (IBM Corp., Armonk, NY) and MedCalc® version 19.1.7 (MedCalc software Ltd., Ostend, Belgium) were used for the statistical analysis. The data are expressed as the mean ± standard deviation. A *P* value < 0.05 was considered statistically significant.

## Results

### Patients

The electronic medical records of 387 patients were reviewed; however, 85 patients were excluded for the following reasons: (1) pain duration of over 12 months (n = 31); (2) affected region was above the T1 dermatome (n = 22); (3) absence of the 3-month follow-up data after the TFESI (n = 32). In final, a total of 302 patients (186 patients in E group and 116 patients in N group) were included in this study (Fig. 1). The patient characteristics of each group are presented in Table 1. There was no significant difference in terms of the patients' gender, age, affected dermatome, pain intensity at the first visit, number of TFESIs, and proportion of the patients with DM and cancer between the two groups (Table 1). The symptom durations of the E group (10.6 ± 17.0 weeks) was shorter than that of the N group (29.3 ± 47.7 weeks) (*P* < 0.001). If the patients received TFESI twice, the mean time interval between the 2 injections showed no significant differences (*P* =

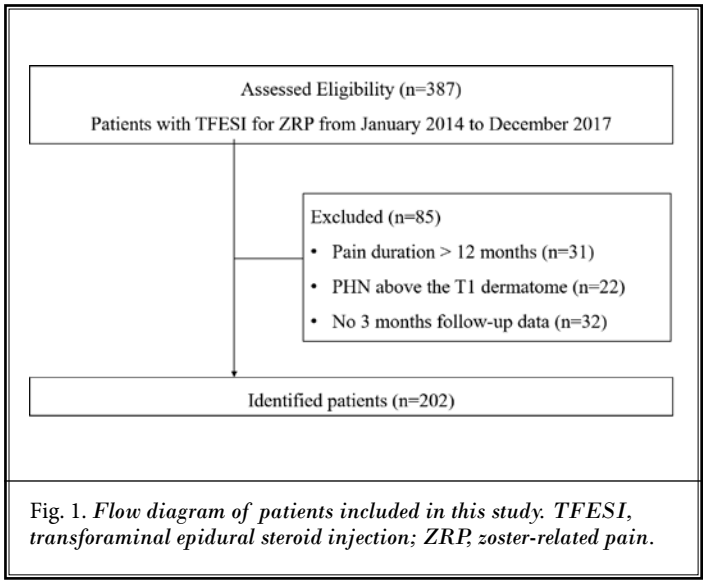


Fig. 1. *Flow diagram of patients included in this study. TFESI, transforaminal epidural steroid injection; ZRP, zoster-related pain.*

Table 1. *Comparison of patient characteristics between the not effective (N) and effective (E) groups after transforaminal epidural steroid injections (TFESIs).*

| Characteristic | E group (n = 186) | N group (n = 116) | *P* values |
|---|---|---|---|
| Gender (M/F) | 76/110 | 49/67 | 0.812 |
| Age (yrs) | 66.8 ± 11.6 | 69.0 ± 10.2 | 0.096 |
| Height (cm) | 156.8 ± 19.2 | 158.2 ± 11.9 | 0.512 |
| Weight (kg) | 63.0 ± 21.9 | 61.4 ± 14.2 | 0.496 |
| Symptom durations (wks) | 10.6 ± 17.0 | 29.3 ± 47.7 | < 0.001* |
| ≤ 12, n (%) | 165 (88.7) | 54 (46.6) | |
| >12, n (%) | 21 (11.3) | 62 (53.4) | |
| Affected dermatome | | | 0.721 |
| Thoracic, n (%) | 162 (87.1) | 103 (88.8) | |
| Lumbar, n (%) | 24 (12.9) | 13 (11.2) | |
| Initial pain (VAS score) | 6.2 ± 1.9 | 6.3 ± 1.9 | 0.632 |
| Number of TFESI | | | 0.523 |
| 1, n (%) | 126 (67.7) | 83 (71.6) | |
| 2, n (%) | 60 (32.3) | 33 (28.4) | |
| Mean time between 2 injections (weeks) | 3.3 ± 0.4 | 3.1 ± 0.8 | 0.594 |
| Medication | | | |
| Strong opioid[a], Yes/No, n (%) | 23 (12.4)/163 (87.6) | 34 (29.3)/82 (70.7) | 0.001[b] |
| MEDD (mg) | 4.3 ±13.8 | 10.6 ± 18.5 | 0.001[b] |
| Nonopioid/weak opioid only[c], Yes/No, n (%) | 110 (59.1)/76 (40.9) | 60 (51.7)/56 (48.3) | 0.233 |
| Anticonvulsant, Yes/No, n (%) | 162 (87.1)/24 (12.9) | 100 (86.2)/16 (13.8) | 0.862 |
| Antidepressant, Yes/No, n (%) | 53 (28.5)/133 (71.5) | 22 (19)/94 (81) | 0.075 |
| Comorbidity | | | |
| DM, Yes/No, n (%) | 35 (18.8)/151 (81.2) | 28 (24.1)/88 (75.9) | 0.309 |
| Cancer, Yes/No, n (%) | 12(6.5)/174 (93.5) | 12(10.3)/104 (89.7) | 0.275 |

Data are reported as the mean ± standard deviation or number (%) of patients.
[a]Strong opioid analgesics included oral morphine, oxycodone, hydromorphone, and fentanyl transdermal patch.
[b]*P* value < 0.05
[c]Nonopioid/weak opioid analgesics included tramadol, acetaminophen, and nonsteroidal anti-inflammatory drugs.
VAS, visual analog scale (0 = no pain; 10 = worst pain imaginable); TFESI, transforaminal epidural steroid injection; MEDD, morphine equivalent daily dose; DM, diabetes mellitus.

0.594) between E (3.3 ± 0.4 weeks) and N (3.1 ± 0.8 weeks) groups. Of the patients in the N group, 29.9% used strong opioids, and there was a significant difference compared to the E group (12.4%, *P* = 0.001). The morphine equivalent daily dose (MEDD) of the N group (10.6 ± 18.5 mg) was higher than that of the E group (4.3 ± 13.8mg) (*P* = 0.001). No statistical differences were observed in terms of the use of other medications for alleviating ZRP (Nonopioid/weak opioids, anticonvulsants, and antidepressants) between both groups.

## The Golden Period for Increased Efficacy of TFESI

The ROC curve analysis showed that a symptom duration of 12 weeks after the onset of HZ was the best cut-off point for predicting the best effectiveness of TFESIs (95% CI: 10-14 weeks), and an area under the ROC curve of 73.8% (95% CI: 0.685-0.787; *P* < 0.001) (Fig. 2).

## The Patient's Factors Associated With the Success of TFESI

Table 2 shows the adjusted ORs with 95% CIs of the patient factors associated with successful TFESI. TFESI was found to be more effective when the symptom duration was ≤ 12 weeks compared with > 12 weeks (OR, 0.107; 95% CI, 0.055-0.205; *P* < 0.001). The positive predictive value at 12 weeks of cut-off time was 75.3%, and the negative predictive value was 74.6%. The patient's sex, age, pain intensity at the first visit, number of TFESIs, presence of DM or cancer, and use of strong opioids were not associated with the effectiveness of TFESI.

## Pain Intensity and Satisfaction of Patients

The difference in baseline VAS scores was not significant (*P* = 0.632, Fig. 3). Both groups exhibited significant decreases in VAS scores from baseline at 2 weeks, 2 months, and 3 months after the TFESI (*P* < 0.001, Fig. 3). Besides, there were significant differences in VAS scores between E and N groups at all-time points during the follow-up period (*P* < 0.001, Fig. 3). The changes (%) in VAS scores from baseline were significantly different between both groups (*P* < 0.001; > 30% in the N group, and > 60% in the E group).

Patient satisfaction scores at 2 weeks, 2 months, and 3 months after the TFESI in both groups are shown in Fig. 4. Significant differences were found in the proportion of patients between N and E groups at all follow-up time points (*P* < 0.001 for 2 weeks, 2 months,

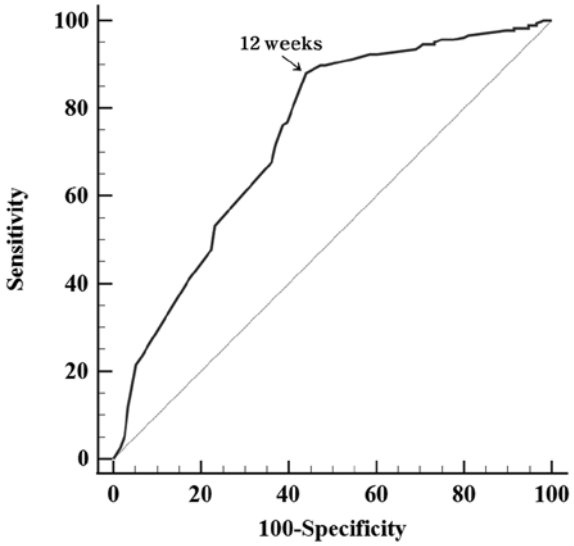


Fig. 2. *Receiver operating characteristic curve for the best cut-off point. The symptom duration of ≤ 12 weeks after herpes zoster onset was determined as the best cut-off point for predicting the effectiveness of the transforaminal epidural steroid injection (sensitivity of 88.17%, specificity of 56.03%) for zoster-related pain. The area under the curve (AUC) is 0.738 (95% confidence interval, 0.685-0.787; P < 0.001).*

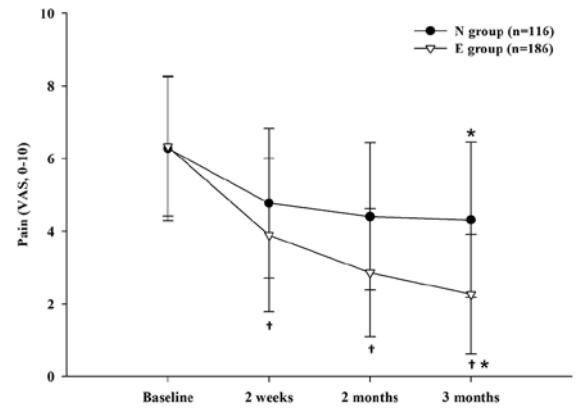


Fig. 3. *Changes in visual analog scale (VAS) scores (0= no pain, 10= the worst pain imaginable) for pain between the N (non-effective) and E (effective) groups. Both groups showed a decrease in pain scores from baseline at 3 months. The E group had a significantly lower VAS score than the N group at each time point. Error bar indicates standard deviation. *Significant at P < 0.001, compared to the baseline VAS score. †Significant at P < 0.001 between E and N groups.*

Table 2. *Odds ratios (ORs) and 95% confidence intervals (CIs) for each variable.*

| Variable | *P* value | OR | 95% CI |
|---|---|---|---|
| Gender | | | |
| Male | - | 1.00 | - |
| Female | 0.913 | 0.970 | 0.565–1.667 |
| Age (yrs) | 0.066 | 0.977 | 0.953-1.002 |
| Symptom duration (wks) | | | |
| > 12 weeks | - | 1.00 | - |
| ≤ 12 weeks | < 0.001 | 0.107 | 0.055–0.205 |
| Severity of initial pain (VAS score) | 0.504 | 0.953 | 0.828-1.097 |
| Number of TFESI | | | |
| 1 | - | 1.00 | - |
| > 1 | 0.250 | 0.707 | 0.391-1.227 |
| DM | | | |
| No | - | 1.00 | - |
| Yes | 0.441 | 1.288 | 0.677-2.451 |
| Cancer | | | |
| No | - | 1.00 | - |
| Yes | 0.075 | 2.358 | 0.917-6.060 |
| Strong opioid | | | |
| No | - | 1.00 | - |
| Yes | 0.770 | 1.117 | 0.533-2.341 |

VAS, visual analog scale (0 = no pain; 10 = worst pain imaginable); TFESI, transforaminal epidural steroid injection; DM, diabetes mellitus.

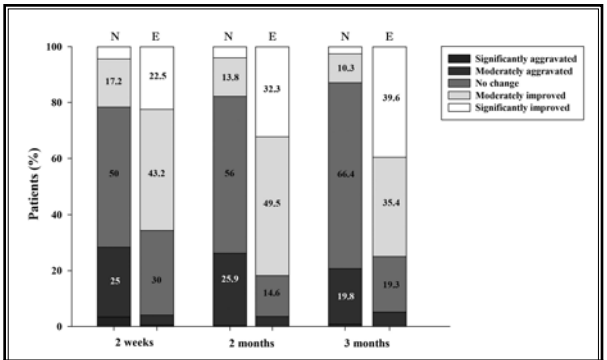


Fig. 4. *Distribution of the 5-point patient satisfaction scores in the N and E groups. The scores were recorded at 2 weeks, 3 weeks, and 6 months of follow-up using a 5-point Likert scale (1 = significantly aggravated; 2 = moderately aggravated; 3 = no change; 4 = moderately improved; 5 = significantly improved). Significant differences were found in the proportion of patients between the N and E groups at all follow-up time points. (P < 0.001 for 2 weeks, 2 months, and 3 months, respectively)*

and 3 months, respectively). In contrast to 75% of patients in the E group, only 11.3% of patients in the N group showed improvement in ZRP at 3 months.

## Discussion

In this study, we found that the best cut-off time point for increased TFESI efficacy to be estimated at 12 weeks after the onset of HZ symptoms. TFESI was more effective when administered within 12 weeks; however, it became less effective when administered after 12 weeks. This is a notable result as patients who have passed the phase of acute herpetic neuralgia can also benefit from receiving TFESI within 12 weeks.

This result is consistent with previous findings that TFESI can prevent or decrease the risk of transition to PHN. Kim and colleagues (12) reported that patients who underwent TFESI within 30 days after the onset of HZ obtained complete pain relief faster compared to those who underwent TFESI between 30 and 90 days. Furthermore, administering an early spinal nerve root block during the acute stage of HZ within 14 days tended to decrease the incidence and shorten the duration of PHN (16). These studies showed a low possibility of transition from HZ to PHN if the TFESI or spinal nerve root block was performed within the acute phase of herpetic neuralgia. Our research found that TFESI effectively relieved pain if performed within 12 weeks after the onset of HZ. This result could indicate the golden period of TFESI for the subacute or chronic stage of ZRP. Furthermore, the results of studies, including ours, showed that earlier treatment of PHN can improve ZRP (9,12). No other studies have analysed the latest effective time of TFESI administration in less than a year after the acute period from the onset of HZ.

In this study, the E group had a significantly lower VAS score and higher patient satisfaction score at all-time points than the N group (Figs. 3 and 4, $P < 0.001$). Moreover, 75% of patients in the E group showed improvements in the ZRP at 3 months. On the other hand, 66.4% of patients in the N group experienced no changes in the ZRP, and the pain even worsened in 19.8% of the patients (Fig. 4). In a previous report, approximately 10% of ZRP patients experienced chronic pain after 6 months, which lasted up to 2 years (2). Chronic ZRP can usually be controlled but not completely cured. In our study, 34% of patients in the N group used strong opioids, which was significantly more compared to the E group (23%, $P = 0.007$). Prescribing opioids for chronic ZRP patients is still controversial (17, 18), but opioids can be considered as rescue drugs for ZRP and should be prescribed carefully by a pain specialist. The proportions of patients using strong opioids and MEDD were higher in the N group than in the E group. However, the effectiveness of TFESI was not related to the use of strong opioids. We can infer that the patients in the N group had the worst pain and therefore were less likely to have a good response to TFESI.

The risk of transition from HZ to PHN is known to be high in older patients, severe HZ lesions, high-intensity pain in the acute phase, ophthalmic involvement, etc (19). In addition, the presence of a severe rash and inflammation caused by HZ can further affect the DRG and adjacent neuronal tissues (5). The role of the DRG, which includes primary sensory afferent neurons, is to transmit peripheral impulses to the spinal cord and central nervous system. If the latent VZV proliferates in the DRG, it can lead to inflammatory neuronal damage and acute ZRP. In addition to these changes in the acute period, the damaged DRG is thought to contribute to pain or chronic ZRP. In a previous autopsy study of the spinal nerve, among all patients with HZ, atrophy of the DRG was only found in patients with PHN (20). Central sensitization of PHN can be preceded by peripheral sensitization. Inflammatory mediators (bradykinin, substance P, histamine, cytokines, etc.) are released from the injured tissue, which leads to a decrease in the threshold of nociceptors (21). Peripheral sensitization leads to an increased and repetitive ectopic discharge of C-fiber nociceptors, which delays the neuronal response in the DRG. These changes contribute to the reorganization of the dorsal horn and thus central sensitization (22). These serial changes do not occur immediately after HZ. Therefore, early TFESI that targets the DRG could prevent the transition from HZ to PHN (12).

Efforts have been made to prevent the transition to PHN by ESI (6). In a study, patients with acute herpetic neuralgia either received interlaminar ESI or only conservative treatment within 7 days after the onset of HZ. Results were that ESI was not effective in preventing long-term pain at 6 months, although it had a modest effect in reducing pain for the first month (6). The reason for this could be the following: interlaminar ESI targets the posterior epidural space, and this method may not deliver the drug to the DRG located in the anterior epidural space. On the other hand, TFESI targets the anterior epidural space, including the spinal nerve root and DRG. Direct drug delivery to the target DRG could block central sensitization causing chronic ZRP. Furthermore, the pulsed radiofrequency (RF) for

PHN directly targets the DRG. Pulsed RF is performed with a transient pulsed RF current and a low temperature (below 45°C) for its neuromodulatory effects (23). This neuromodulatory effect induced by pulsed RF could last for 3 months after the procedure (24). Kim and colleagues reported that the pulsed RF group had higher pain relief than the control group for 90 days when administered within 90 days after the onset of HZ (25). In another study, the pulsed RF group experienced longer-lasting pain relief and showed an 88% effective treatment rate (23). Therefore, early pulsed RF for the treatment of PHN was also recommended.

Another study assessed the effect of nerve block in the early phase of HZ. Ji and colleagues (26) reported that repetitive paravertebral block reduced the incidence of PHN at the 1-year follow up. The paravertebral block usually can be applied for ZRP at the thoracic vertebral level, and the drug is injected into the paravertebral space to block spinal nerves as they emerge from the intervertebral foramen. They chose patients in the acute phase of HZ within 7 days after the onset, and the paravertebral block was performed every 48 hours for a week. The repetitive paravertebral block group had a significantly reduced incidence of PHN than the medication-only group. This study also showed that early management for HZ was important for reducing the incidence of PHN.

There are several limitations to this study. Firstly, this study was not a prospective randomized controlled trial (RCT). However, the purpose of this study was to identify the cut-off time points for effective TFESI treatment and to identify factors that affect treatment efficacy. Therefore, although not an RCT, the results of this study are meaningful. Secondly, there was no comparison with a conservative treatment group. We were unable to distinguish the effects of TFESI with the natural healing process. However, many aforementioned studies showed that nerve blocks for treating ZRP in the early phase were superior to the conservative treatment (7,12,13). Thirdly, the follow-up period was only 3 months. It was difficult to elucidate the actual duration of pain reduction due to this short follow-up period. Further long-term follow-up studies are required. Finally, we only used VAS scores and global satisfaction of the patients rather than the multi-dimensional pain questionnaire for measuring the effectiveness of the TFESI. The pain characteristics of ZRP experienced by patients are very complex. A multi-dimensional pain questionnaire would have yielded more accurate results.

Although our study had the aforementioned limitations, it demonstrated that symptom duration in patients with ZRP was the most important indicator of the effectiveness of TFESI. Therefore, the clinical challenge is to shorten the duration of the symptoms. This result supports the hypothesis that there is a tendency for unfavorable treatment outcomes when ZRP is treated after it becomes chronic.

In conclusion, our results demonstrated that TFESI is an effective and safe method for the treatment of patients with ZRP, particularly within 12 weeks after HZ onset. Further prospective randomized controlled trials of TFESI and a comparative study with conservative treatment should be conducted to confirm the efficacy of this treatment in patients with HZ-related pain.

## Acknowledgments

The authors thank Ms. Mihee Park of Seoul National Bundang Hospital for her illustration work in this study.

## Author Contributions

EC conducted the statistical analysis and wrote the manuscript. FSN designed the study protocol and provided final approval of the manuscript. WKH, PL, and HJ revised the manuscript for intellectual contents. HL conducted the statistical analysis. HYG and JHK contributed to the acquisition and interpretation of data. All authors have read and approved the final manuscript.

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