Original Article

A Randomized clinical trial comparing the efficacy of ultrasound-guided erector spinae block and paravertebral block in preventing postherpetic neuralgia in patients with zoster-associated pain

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Abstract

Background and Aims: The treatment for postherpetic neuralgia (PHN) continues to be challenging in clinical pain management. Paravertebral block (PVB) and erector-spinae block (ESPB) are two novel techniques for treating this distressing condition. We aimed to assess the effectiveness of PVB and ESPB in preventing the progression to PHN in patients with acute herpes zoster (AHZ).

Material and Methods: Sixty patients in pain due to AHZ were selected for a prospective randomized control study after approval from Institutional Ethical Committee. Written informed consent was taken. Patients were randomized and allotted into Control-group: standard treatment (oral antivirals, analgesics, neuropathic medicines); PVB-Group: standard treatment with PVB and ESPB- Group: standard treatment with ESPB. Under ultrasound guidance, both blocks were administered with 20 ml of 0.25% bupivacaine + dexamethasone 8 mg. Efficacy was evaluated on the 15th, 30th, and 60th day post treatment. The primary endpoint was the proportion of patients with adequate relief from pain and allodynia post study.

Results: The incidence of PHN post study was 45% in the ESPB group and 40% in the PVB group and 80% in the control group (p = 0.022). The proportion of patients with pain relief was higher among the PVB group compared to the ESPB group but not statistically significant (p 0.749). On day 60, the mean pain score was 2.45 (±3.05) and 2.15 (±2.7) in ESPB and PVB groups, respectively, and 4.3 (±2.27) in the control group (p 0.003).

Conclusion: PVB and ESPB are effective approaches in treating patients suffering from pain due to acute zoster and help in preventing its progression to PHN.

Keywords: Erector spinae plane block, paravertebral block, post herpetic neuralgia, ultrasound

Introduction

The very crippling sign of pain can have an impact on many facets of life, including the physical, psychological, and vocational aspects. Herpes zoster (HZ) infection produces pain that is extremely challenging to treat because it is resistant to conventional pharmaceutical modalities. After initial infection, the Varicella Zoster virus stays dormant in the body and, upon reactivation, results in HZ which causes

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a variety of symptoms including dermatomal skin rashes, vesicles, paresthesia, and the most noticeable symptom, pain.[1] Post-herpetic neuralgia (PHN) is more likely to develop if the original pain is more intense. A 5–50% incidence of PHN is present. This large range is explained by the various study designs, definitions, and age distributions considered by various studies.[2–5] All of these simply serve to emphasize how crucial it is to treat the first pain aggressively to avoid the development of PHN and the ensuing impairments. With encouraging outcomes, two novel interfascial nerve blocks have recently been used: the paravertebral block (PVB) and the erector spinae block (ESP). Only single case reports or observational studies, however, exist for any of the two procedures.[1,5–9] Few studies have compared the outcomes of the two approaches in patients with acute HZ.[10] To examine the effectiveness and success of PVB and erector spinae plane block (ESPB) in treating pain, enhancing the quality of life, and preventing PHN in patients with acute HZ, we undertook this study. Our primary objective was to compare the effectiveness of PVB and ESPB in treating zoster-related pain (ZP) and preventing the progression of ZP to PHN. Secondary objectives were to compare the safety, practicality, and convenience of the two blocks; assess any complications like bleeding, nerve injury, and local anesthetic toxicity due to the blocks; and compare the changes in quality of life in patients affected with zoster before and after administering PVB and ESPB.

Material and Methods

A single-blind, parallel arm, prospective randomized clinical trial with a 2-month follow-up period was conducted in our tertiary center after approval by the institutional ethics committee. (Approval number: JSS/MC/PG/5189/2019-20). The study was enrolled in the Clinical Trial Registry of India (Clinical trial registration number: CTRI/2021/01/030258). With the confidence interval of 95% and 80% power, considering the difference in the percentage of pain relief between two study groups based on a study conducted by Genlin Ji *et al.*[11] was 23%, the sample size was estimated to be n ≈ 16 in each group. Taking into consideration any possible dropouts, we selected a sample size of 20 in each group. Patients with features suggestive of acute HZ were referred from the dermatology department to our pain clinic. We defined acute HZ as a painful skin rash of less than one-month duration, with blisters/rashes in a limited area on one side of the body. Criteria for inclusion were patients belonging to the American Society of Anaesthesiology Physical class I, II, and III, presenting with pain in acute stages of HZ, confined to the thoracolumbar region, in the age group of 20–80 years, and with pain severity of 5 or more on Numerical Rating Score (NRS). We excluded pregnant women and patients with infection at the local site, a history of allergy to local anesthetics, uncontrolled diabetes, psychiatric diseases, and bleeding diathesis. A thorough medical history was obtained with particular attention to pain characteristics such as onset, duration, site, and character of pain along with its aggravating and relieving factors. Psychological changes due to the pain and presence of allodynia were noted using the second domain of the WHOQOL pilot assessment domains and facets.[12] This considers the patient's positive feelings, thinking, learning, memory and concentration, self-esteem, bodily image and appearance, and negative feeling.[12] Pain was assessed using NRS. This consists of a horizontal line with an eleven-point numeric range marked from zero to ten, with zero indicating no pain and ten being the worst pain possible. Quality of life was assessed using the physical health domain of the World Health Organization's (WHO) quality of life (WHOQOL) scale. This scores the patients based on their activities of daily living, dependence on medical substances and aids, energy and fatigue, mobility, pain and discomfort, sleep, rest, and work capacity.[12] Previous treatments, significant medical history, and personal history were also noted. A local examination of the skin lesions was done and dermatomes were marked. Sixty patients assessed to be eligible for the study were informed about the procedure and written informed consent was obtained. With patients still on their respective treatment protocols as directed by dermatologists, they were divided into three groups by computer-generated randomization.

On the day of the procedure, after explaining the procedure under ultrasound guidance and obtaining consent, the patient was taken to the procedure room. An intravenous line was secured and fluid infusion with ringer lactate was started. Basic monitors (heart rate, noninvasive blood pressure, electrocardiogram, oxygen saturation (SpO2)) were connected. Patients were positioned prone, and under all sterile precautions, blocks were administered with ultrasound guidance.

The level of administration of PVB or ESPB was determined by considering the dermatomes affected with pain and skin lesions. The ESPB group received ultrasound-guided ESPB with 20 ml of bupivacaine 0.25% and 8 mg of dexamethasone. A high-frequency linear transducer was used for administering blocks at the thoracic level and a convex transducer was opted for blocks at the lumbar level. The probe was placed in the transverse orientation of the desired spinous process and moved laterally for 3 cm until the transverse process (TP) was identified. The probe was then rotated by 90 degrees. A 22 gauge Quincke spinal needle, passed in plane, was used for administering blocks. Trapezius, rhomboid major (until T7), and erector spinae muscles were identified with the TP as a landmark, and the needle was advanced in a cephalad to caudal direction through these muscles to gently contact the TP. After gentle aspiration, hydro dissection was done and 20 ml of 0.25% bupivacaine and 8 mg

of dexamethasone were deposited in the fascial plane, deeper to erector spinae muscle at the tip of the TP of the vertebra.

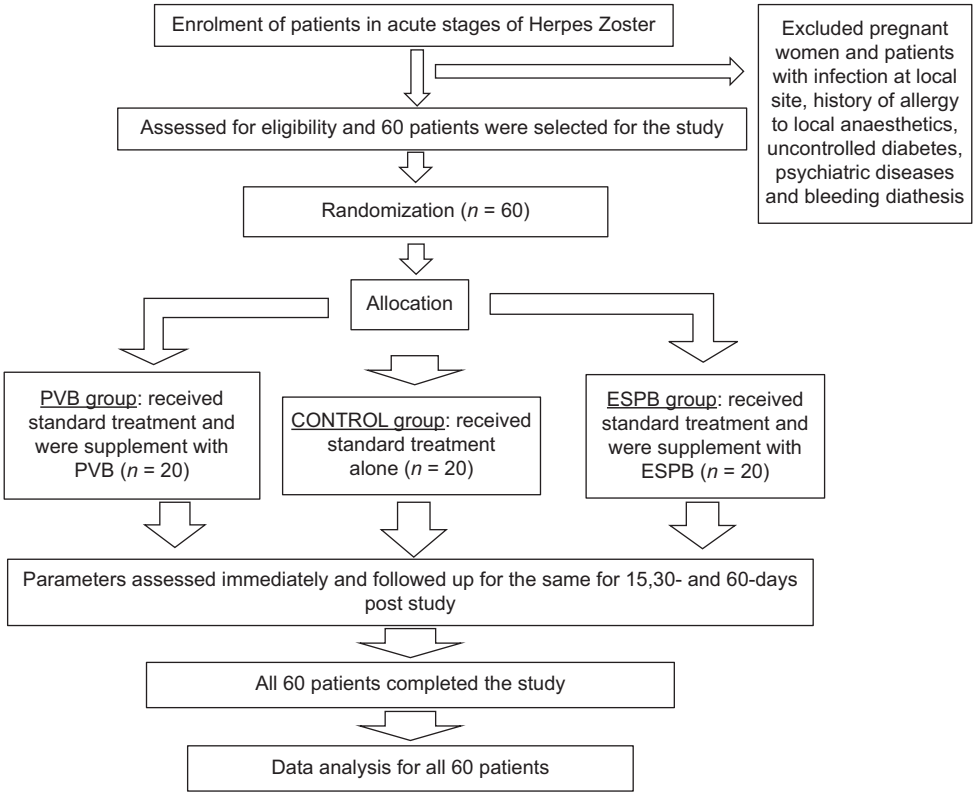
PVB group received ultrasound-guided PVB with 20 ml of bupivacaine 0.25% and 8 mg of dexamethasone. The probe was placed along the transverse direction of the desired spinous process and then moved laterally for 3 cm until the TP was noted. The probe was then rotated by 90 degrees. Pleura, TP, paravertebral space, superior costotransverse ligament, trapezius, rhomboidus, and erector spinae muscles were identified. A 22-gauge Quincke spinal needle was advanced perpendicular to the skin to contact the TP of the vertebra. This was achieved by manipulating the needle in a cephalad and caudad direction at the same depth until the bone was encountered. The needle was then walked above the TP and gradually advanced until a loss of resistance to saline or a subtle pop was felt as the tip of the needle traversed the superior costotransverse ligament. After gentle aspiration, 20 ml of 0.25% bupivacaine and 8 mg of dexamethasone were deposited in the paravertebral space. The control group received standard treatment alone as per the institutional protocol followed by dermatologists.

After administering the block, patients were monitored and assessed for pain relief with NRS for a period of 2 h. Secondary characteristics of pain such as general condition, pulse rate and rhythm, respiratory rate, and blood pressure were monitored. We used a spirit-soaked cotton swab to assess the number of segments covered by the block. Post procedure, patients were prescribed rescue analgesia to be taken only if necessary. If the block failed, rescue analgesia was given with a slow intravenous injection of tramadol 50 mg. The rescue analgesic advised to be taken at home was the combination tablet of paracetamol + tramadol along with tablet ondansetron 4 mg for pain relief.

The patients were followed up on days 15, 30, and 60 post block and assessed for pain relief using NRS; any progression to PHN; improvement in quality of life using the WHOQOL scale; and the need for rescue analgesia. Every visit and follow-up were documented, and results were tabulated and analyzed at the end of 60 days. Incidence of PHN was assessed as persistent pain and/or allodynia, and "abnormal sensations" (hypoesthesia, burning, itching, etc.) by the end of the study.

Data were entered into a Microsoft Excel data sheet and analyzed using SPSS 22 version software. Categorical data were represented in the form of frequencies and proportions. The Chi-square test was used as a test of significance for qualitative data. Continuous data were represented as mean and standard deviation. ANOVA was used to test the significance of continuous variables. A P value (probability that the result is true) of <0.05 was considered statistically significant after assuming all the rules of statistical tests.

Consort flow chart



Results

Sixty patients were enrolled in the study, randomized and equally allocated to the three groups with 20 in each group. Demographic details and baseline characteristics of the patients did not differ significantly among the three groups [Table 1].

The results of the primary and secondary objectives are mentioned in Table 2. A significant decrease in the intensity of pain was observed among the patients following the block when compared to the control group. This was assessed by the changes in the NRS values measured at different intervals. Patients had basal NRS 8 (1.17) in the PVB group, 7.70 (1.12) in the ESPB group, and 7.50 (1.19) in the control group before the study (statistically insignificant). On the 30th day following the block, NRS in PVB, ESPB, and control group were 3.750 (2.3), 3.40 (2.6), and 6.15 (0.74), respectively, and on the 60th day, it was 2.15 (2.7), 2.45 (3.05), 4.30 (2.27), respectively, indicating a statistically significant reduction in pain ($p = 0.003$).

Table 1: Comparison of baseline demographics between study groups

	ESPB group	PVB group	Control group	*P*
Age in years (SD)	56.10 (12.47)	49.40 (13.86)	57.60 (9.48)	0.7
Sex male: female	15:5	7:13	11:9	

ESPB: Erector spinae plane block; PVB: Paravertebral block; SD: Standard deviation

The patients were enquired about the analgesic tablets they consumed at home after receiving the block (rescue analgesia). The number of days per week that they needed rescue analgesia was noted. It was observed that there was decreased need for rescue analgesia in the groups receiving ESPB and PVB when compared with the control group. By end of the study period, the mean (SD) days per week for rescue analgesic requirement was 2.15 (2.70), 2.10 (2.92), and 4.20 (2.13) in ESPB, PVB, and control groups, respectively,

Significant improvement in quality-of-life following treatments was observed in ESPB and PVB groups when compared with the control group. The mean quality of life score of participants belonging to the ESPB group was 73.35 (vs basal score of 29.90) and PVB group was 76.10 (vs basal score of 35) and the control group was 47.25 (vs basal score of 23.90). The incidence of PHN by the end of study was 45% in the ESPB group and 40% in the PVB group and 80% in the control group. Psychological changes could not be tabulated for comparison as the replies were vague and could not be quantified appropriately. No adverse events were noticed during or after our study.

In our study, when we separately analyzed the mean pain scores, a significant reduction as measured by a decrease in NRS from the baseline was noted in both ESPB (decrease to 2.85 from 7.70 in NRS at 2 h post procedure, $P < 0.0001$ and further decrease to NRS 2.45 by the end of study,

Table 2: Comparison of outcome parameters among the study groups

	ESPB group	PVB group	Control group	*P*
The proportion of patients with pain relief (%) (NRS<3)	55	60	20	0.022*
Incidence of PHN (%)	45	40	80	0.022*
Segments blocked	5.15 (1.26)	5 (1.21)	NA	<0.704
Duration of analgesia (hours)	15.2 (3.91)	13.1 (2.64)	NA	0.079
Pain scores (as per NRS) across the study period				
Before study	7.70 (1.12)	8 (1.17)	7.50 (1.19)	0.39
Immediate post procedure	2.85 (1.89)	3.9 (1.65)	7.30 (1.12)	0.07
After 15 days	3.30 (2.2)	3.85 (2.3)	6.15 (0.7)	<0.001*
After 30 days	3.40 (2.6)	3.75 (2.3)	6.15 (0.74)	<0.001*
After 60 days	2.45 (3.05)	2.15 (2.7)	4.30 (2.27)	0.003
% Of allodynia among patients present after intervention				
After 15 days	25	40	55	0.153
After 30 days	20	15	40	0.155
After 60 days	15	10	40	0.04*
Requirement of rescue analgesia after intervention (Days/week)				
After 15 days	3.70 (1.83)	3.75 (1.94)	5.05 (0.60)	0.013*
After 30 days	2.85 (2.66)	2.50 (1.35)	4.6 (1.31)	0.001*
After 60 days	2.15 (2.70)	2.10 (2.92)	4.20 (2.13)	0.001*
Quality of life				
Before intervention	29.90	35	23.90	<0.001*
After intervention (60 days post intervention)	73.35 (9.02)	76.10 (9.42)	(20.85)	

**Statistically significant difference at P<0.05. ESPB: Erector spinae plane block; PVB: Paravertebral block*

$P < 0.0001$) and PVB groups (decrease to 3.90 from 8 in NRS at 2 h post procedure, $P < 0.0001$ and further decrease to NRS 2.15 by the end of study, $P < 0.0001$). The mean time of duration of analgesia (h) among the ESPB group was 15.2, more than the PVB group, 13.1, though not statistically significant.

Discussion

This study was taken up to evaluate the efficacy of the two blocks – ESPB and PVB – in relieving pain, improving the quality of life, and preventing progression to PHN, and we found promising results with both techniques. We enrolled 20 patients in each group of our study and found improvement in pain scores in the PVB and ESPB groups when compared to the control group. The incidence of PHN was 45% in the ESPB group, and 40% in the PVB group compared to 80% in the control group.

Zoster-related pain (ZP) is a dreaded symptom with a poorly understood pathophysiology. The local inflammation of the dorsal root ganglion lays the foundation for a later PHN, especially if the initial pain is inadequately treated.[6] Several mechanisms have been proposed. "Sensitization mechanism" explains how inflammatory mediators alter the responses of sensory neurons and lower the threshold of nociceptors. These irritable nociceptors induce and maintain sensitization. Inflammatory swelling causing nervous tissue ischemia by compression effect on the sensory ganglia forms the basis of the "deafferentation mechanism". Loss of nociceptive afferents due to massive degeneration and synaptic reorganization are some of the other proposed mechanisms of ZP.[1,9] The standard treatment with analgesics, corticosteroids, antidepressants, anticonvulsants, and opioids may not prevent and treat PHN always.[5] Nerve blocks such as the PVB and ESPB are microinvasive methods found to provide effective pain relief and also prevent progression to PHN.

The PVB is a simple block involving the deposition of the drug in the paravertebral space identified by the loss of resistance encountered after walking the needle off the tip of the TP. The mechanism of PVB is by direct penetration of the local anesthetic into the dorsal rami, spinal nerve, rami communicants, and the sympathetic chain. This blocks the transduction of pain rostrally, completely abolishes somatosensory evoked potentials, prevents central sensitization, and provides analgesia. The steroid has an anti-inflammatory and membrane-stabilizing effect on the C fibers. They prevent disease progression by suppressing ectopic neural discharges and blocking nociceptive input transmission. Makharita MY *et al.*[13] report the epidural spread of a radio-opaque dye in 74.3% of their patients when they injected the dye to confirm the proper placement of the needle in paravertebral space. Several other studies too report the epidural spread of drugs in PVB.[14–16] This epidural spread of local anesthetic and steroids probably explains the rapid pain relief seen.[13] Interestingly, direct epidural injection of the drug has not shown promising results in the prevention of PHN as reported by the PINE study and a few other studies.[17] PVB, thus, provides a superior quality of block compared to central neuraxial techniques while avoiding the complications of these techniques.[13,16] The dense sympathetic blockade by PVB not only suppresses the afferent inputs but also promotes early resolution of skin lesions by causing vasodilatation and improving blood flow to the affected dermatome.[6,13]

In our study, we found a significant decrease in pain scores with a single injection of PVB, from a basal NRS of 8 (1.17) before block administration, to 3.750 (2.3) on day 30 and 2.15 (2.7) on day 60. A similar finding of shorter pain duration in patients who received PVB was reported by Makharita MY *et al.*[13] in their study. Genlin Ji *et al.*[11] found that repetitive PVB injections with local anesthetic and steroids significantly reduced the incidence of PHN when compared with standard treatment alone, with a $P < 0.001$ at one month following therapy. A time-sensitive efficacy of repetitive PVB with better pain relief and sleep quality in acute and subacute cases of HZ than in chronic patients has also been reported.[6]

The ESPB is a novel analgesic technique first described by Forero *et al.*[7] It involves the deposition of drugs in the interfascial plane between the rhomboid major and erector spinae muscles. The observed analgesic effect is thought to be due to the diffusion of the local anesthetic into the paravertebral and intercostal spaces, blocking the dorsal and ventral rami of spinal nerves along the way. ESPB also offers the advantage of a wide spread of the block, covering between three to eight dermatomes with 20 ml volume as evidenced in radiological and cadaveric studies.[5,7,8] In our study, the mean (SD) number of segments blocked were 5.15 (1.26) in the ESPB group and 5 (1.21) in the PVB group, with no statistical significance. There was also significant pain relief experienced with this block with a basal NRS of 7.70 (1.12) before the block and NRS of 3.40 (2.6) on day 30 and 2.45 (3.05) on day 60. Our findings are in concordance with the results obtained in the study by Aydın *et al.*[5] who administered single injection for acute cases and continuous blocks for chronic pain. ESPB can be administered in not just the thoracic and lumbar areas but also the cervical region for ZP. It has a low complication rate, can be done even in ambulatory settings, has easy sonographic identification, and has multiple indications besides treating ZP.[9]

The decreased incidence of PHN noticed in our study may be related to the multiple mechanisms of action of PVB and ESPB mentioned earlier. The improvement in quality of life and the decreased requirement of rescue analgesic consumption were comparable among both the groups during and after the study period denoting equal efficacy of both ESPB and PVB in treating HZ pain. Both the blocks were administered under ultrasound guidance and our operators reported relatively more ease in administering ESPB compared to PVB stating the relatively decreased depth and presence of lesser critical structures in the vicinity as the main reasons. A similar study has been conducted by Abdelwahab EH *et al.*[10] at around the same time as our study was conducted. They compared the success of ESPB and PVB in the Egyptian population by using only 2.5 ml of 0.5% bupivacaine made to 10 ml along with 8 mg of dexamethasone and using acetaminophen for rescue analgesia. They too noted a similar efficacy in both blocks when compared to the control group in controlling the acute pain of HZ.

The main limitations of our study are the small sample size, lack of double blinding, and relatively short period of follow-up. Though ours is a tertiary center, it caters mainly to the rural population in the surrounding areas. It has been our experience that the patients do not turn up regularly for follow-up due to financial, domestic, and other constraints. Hence, we decided to conduct our study using a single shot technique and opted for a follow-up of up to only 60 days.

Conclusion

Both PVB and ESPB are effective, feasible, and safe modalities for preventing the progression and exaggeration of ZP when administered in acute phases with a local anesthetic and steroid combination. It shortens the pain duration, improves the quality of life, reduces the need for rescue analgesics, and lowers the incidence of PHN.

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Conflicts of interest
There are no conflicts of interest.

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