Clinical Pain Research

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Application of ultrasound-guided thoracic paravertebral block or intercostal nerve block for acute herpes zoster and prevention of post-herpetic neuralgia: A case–control retrospective trial

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Abstract

Objectives – Ultrasound (US)-guided intercostal nerve block (ICNB) is an easier approach with a very low incidence of complications for different surgeries; nevertheless, only a few studies estimate the effect of ICNB for acute HZ. To explore the US-guided ICNB for management of herpes zoster (HZ)-related acute pain and possible prophylaxis for post-herpetic neuralgia (PHN) taking the conventional thoracic paraverteral block (TPVB) as control.

Methods – A total of 128 patients with HZ were retrospectively stratified into antiviral treatment (AVT) plus US-guided TPVB (TPVB group), AVT plus US-guided ICNB (ICNB group) or AVT alone (control group) based on the treatment they received. HZ-related illness burden (HZ-BOI) over 30 days after inclusion as the primary endpoint was determined by a severity-by-duration composite pain assessment. Rescue analgesic requirement, health-related quality of life, PHN incidence, and adverse events were also recorded.

Results – Significantly lower HZ-BOI scores within post-procedural 30 days using the area under the curve were reported with TPVB and ICNB compared with the control group: mean difference of 57.5 ($p < 0.001$) and 40.3 ($p = 0.003$). No difference was reported between TPVB and ICNB ($p = 1.01$). Significant greater improvements in PHN incidence, EQ-5D-3L scores, and rescue analgesic requirements were observed during follow-up favoring two trial groups, while comparable between two trial groups. No serious adverse events were observed.

Conclusions – US-guided ICNBs were as effective as TPVBs for acute HZ. The ICNB technique was an easier and time-efficient approach as opposed to conventional TPVB, which might be encouraged as a more accessible preemptive mean for preventing PHN.

Keywords: ultrasound-guided thoracic paravertebral block, ultrasound-guided intercostal nerve block, herpes zoster-associated acute pain, post-herpetic neuralgia, herpes zoster burden of illness

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Abbreviations

US	ultrasound
TPVB	thoracic paravertebral block
ICNB	intercostal nerve block
AVT	antiviral treatment
PHN	post-herpetic neuralgia
HZ	herpes zoster
BOI	burden of illness
QoL	quality of life
VZV	varicella zoster viruses
ZAP	zoster-associated pain
ZBPI	Zoster Brief Pain Inventory

AUC area under the curve
LA Local anesthetics
ANOVA analysis of variance.

1 Introduction

Herpes zoster (HZ) is characterized by a unilateral band-like vesicular rash in the dermatome that corresponds to the affected nerve caused by a reactivation of latent varicella zoster viruses (VZV) [1]. The lifetime risk of HZ in the general population is from 20 to 30% but increases dramatically over 50 years of age reaching 50% at 85 years [2]. During the acute episode, the goal of treatment is to reduce the intensity and duration of symptom and prevent complications. Post-herpetic neuralgia (PHN) defined as acute zoster-related pain (ZAP) sustaining for at least 90 days after rash is a debilitating complication of HZ and becomes more common with increasing age, about 5–20% in those aged younger than 60–80 years or older according to a large population-based study [3]. Unfortunately, there is no reliable intervention that relieves the pain of PHN up to now. Therefore, effective treatments for preventing PHN have become an important focus of the current study. Epidemiological research showed that interventions aimed to decrease the repetitive painful stimuli and inflammation during the acute HZ might attenuate central sensitization to reduce the prevalence of PHN [4]. In this respect, ultrasound (US)-guided paravertebral block (PVB) has been successfully used in resolving pain in acute HZ and is capable of preventing the incidence of PHN [5–7]. Compared with the PVB technique, intercostal nerve block (ICNB) under US guidance is an easier superficial block with a very low incidence of complications for different surgeries involving the chest wall and rib fractures [8]. However, to our knowledge, only one comparative trial with a very small sample estimated the effect of ICNB for acute HZ [9]. Therefore, this study was designed to test the hypothesis that repetitive ICNB under US guidance during the acute phase could provide comparable acute pain management and PHN prevention in patients presenting with thoracic HZ as the most frequently involved dermatome. The ICNB technique also has a more time-efficient approach and a better side effect profile as compared to thoracic PVB.

2 Materials and methods

2.1 Study design

This present study was conducted as a case–control retrospective trial according to the principles of the Declaration of Helsinki and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [10]. The protocol of the study was approved by the Clinical Research Ethics Committee of Beijing Chuiyangliu Hospital (2023-015KY) and registered in the Chinese Registry of Clinical Trials (ChiCTR2300076442). Written informed consent about data for publication was obtained from all participants before enrollment.

Between January 1, 2022, and April 30, 2023, patients who attended our pain clinic of anesthesiology department for the treatment of thoracic herpetic eruption were reviewed and divided into the following groups depending on the treatment they received (Figure 1). The control group received a standard 7-day course antiviral treatment (AVT) (valacyclovir 0.3 g, three times daily) immediately after enrollment. The thoracic paraverteral block (TPVB) group received the same AVT and the US-guided repeated TPVB injections following AVT. The ICNB group received the AVT plus the subsequent US-guided repeated ICNB. Injection was repeated every 48 h for a week up to 4 times. Celecoxib and oxycodone and acetaminophen were offered on request as rescue analgesic according to pain intensity assessed by Zoster Brief Pain Inventory (ZBPI) at a dosage of 200 mg tablets, up to 2 times daily, and 5 mg:325 mg tablets, up to 4 times daily, respectively, whereas antidepressant or antiepileptic drugs and other nerve blocks including epidural or intrathecal blocks were prohibited.

2.2 Participants

The inclusion criteria were as follows: (1) HZ-related acute pain originating from thoracic; (2) shorter than 4-week duration from initial rash onset; (3) moderate-to-severe pain; and (4) age 50 years or older. Patients who had immunity impairment, hepatic or renal dysfunction, coagulopathy, cognitive disorders, analgesic addition, pregnancy/lactation, and incomplete medical data were excluded.

2.3 Procedures description

All procedures were performed by four senior pain doctors who were proficient in performing US-guided peripheral nerve block procedures. Standard monitoring was applied in the form of electrocardiography, blood pressure, and oxygen saturation.

2.4 US-guided TPVB procedure

A low-frequency convex array US probe (2–5 MHz) was placed on a transverse position parallel to the spinous

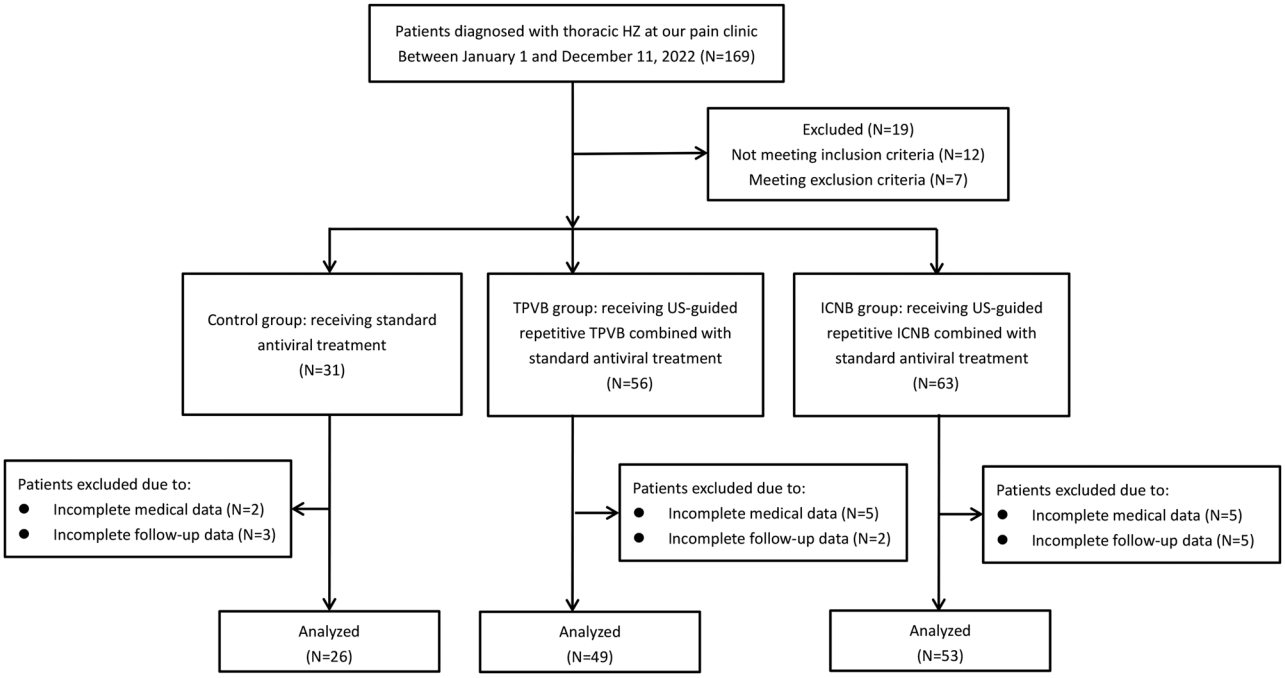

Figure 1: The diagram of patient recruitment.

process of the targeted thoracic segment, to achieve a transverse axis view of the vertebral plate and transverse process (TP) recognized as a hyper-echoic structure with anterior dark acoustic shadow. Then, the probe was slightly moved to the caudal direction until the above-mentioned typical images disappeared. Parts of thoracic paravertebral space were visualized among the hyperechoic image of parietal pleura, superior costotransverse ligament, and internal intercostal membrane. A 22-G needle was inserted from the lateral to the targeted TPVB using the in-plane technique after verification of no vulnerable blood vessel abnormally situated in the puncture path with color Doppler mode (Figure 2a). After negative aspiration, 1 ml of 1% lidocaine was injected as the experimental dose. After observation of anesthesia or pain alleviation in the affected dermatomal without any adverse events, a single 5 ml mixture comprising 0.5% lidocaine, 1 mg/ml triamcinolone, and normal saline was injected under real-time US guidance. Subsequently, the anterior displacement of the pleura and the widening of the paravertebral space (PVS) were visualized in the US scan confirming a correct injection.

2.5 US-guided ICNB procedure

In this technique, the same low-frequency transducer was positioned 3–4 cm lateral away from the midline after identification of the targeted intercostal space. Two adjacent ribs were seen as hyperechoic and its characteristic rounded structures in the sagittal US image. An acoustic window was clearly visualized by reflections from the intercostal ligaments, the intercostal space, and the parietal pleura between the acoustic shadows of two ribs. Using Doppler US, the intercostal vessels were readily visible at the lower margin of the upper rib in the intercostal space. Additionally, the targeted intercostal nerve root was lying beneath the color Doppler signal from the intercostal artery (Figure 2b). The same 22-G block needle was inserted in the plane of the real-time US beam. The same experimental lidocaine was injected after negative aspiration to confirm anesthesia/pain alleviation in the affected dermatomal without any side effects. The success of block was achieved with the same therapeutic injection and subsequent distribution along the intercostal space on the sagittal axis view.

2.6 Outcome measures and data collection

Pain severity was evaluated using an 11-point scale Likert scale (0–10) which was derived from question 3 of the ZBPI to rate “the worst pain during the last 24 h” [11]. The burden of illness (BOI) score was developed as the severity and duration of HZ disease. It was calculated from the above-mentioned ZBPI worst pain scores over the predefined follow-up days from the first day of HZ rash onset (D0) using the area under the curve (AUC) by GraphPad

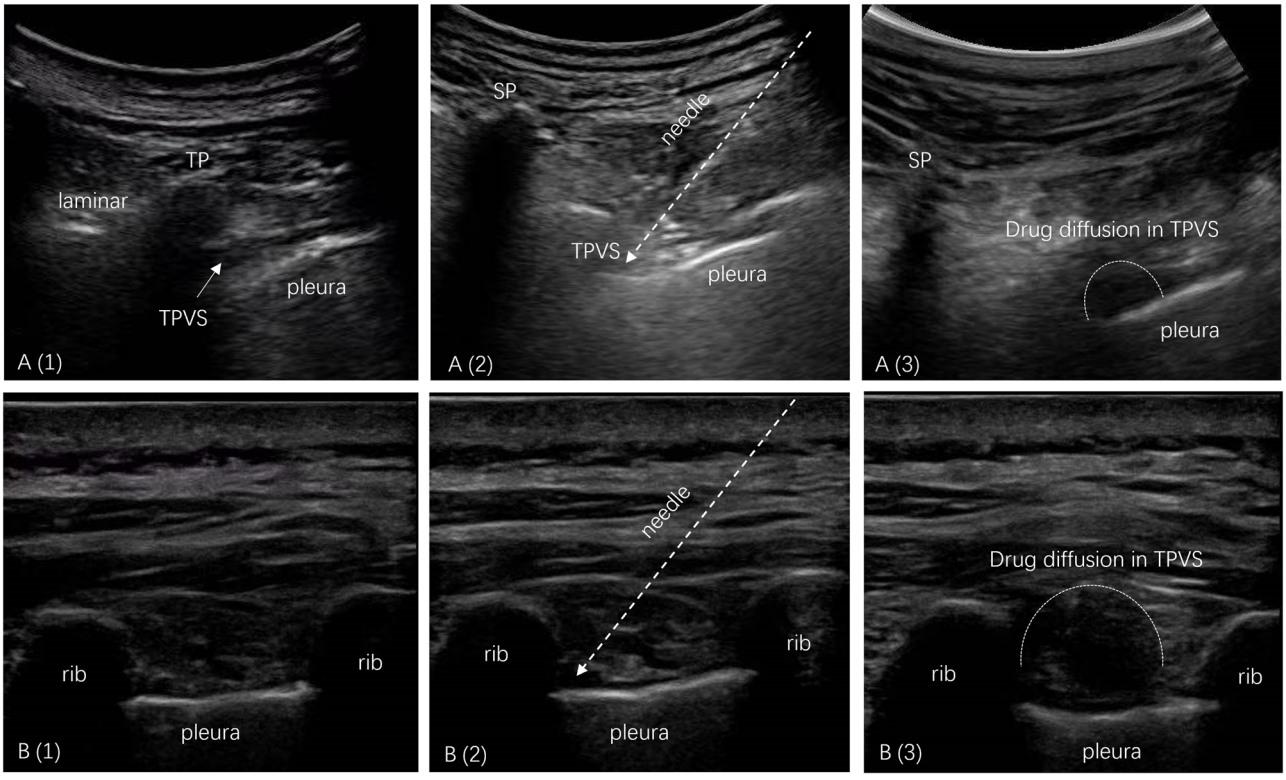

Figure 2: (a) (1–3) Thoracic paravertebral block under US guidance. (b) (1–3) Intercostal nerve block under US guidance. SP = spinous process; TP = transverse process; TPVS = thoracic paravertebral space; US = ultrasound.

Prism version 5.0 (GraphPad Software Inc., San Diego, CA) based on the multiple segment trapezoidal rule [12]. The EuroQoL 5-Dimension questionnaire (EQ-5D-3L) was employed to assess the health-related quality of life (HR-QoL), which recorded self-reported problems on each of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension was divided into three levels including no problems, some problems, and extreme problems [13]. PHN was pre-defined as ZBPI "worst pain" persisting 90 days after rash onset according to clinical diagnostic criteria [14]. The consumption of concomitant analgesics was also recorded. Safety was assessed by adverse events.

The primary endpoint was HZ-related BOI scores over 30 days (HZ-BOI-AUC_{30}). Follow-ups were conducted every week for the first month (on days 7 [D7], 14 [D14], 21 [D21], 30 [D30]) at the pain clinic and then in 3-month intervals for 6 months via telephone by two special trained nurses who were blinded to the patients' assignment.

2.7 Sample size calculation

The study derived the efficacy statistic based on BOI-AUC_{30} scores. According to data about BOI-AUC_{30} with a mean of 110 and standard deviation (SD) = 20–35 by 5 with AVT alone in published research [6], we wanted to detect a shift in the mean of at least 20% decrease in two peripheral nerve block groups. To accomplish this, the mean of the control group was set to 0 and the other two intervention means to 33 using PASS version 16.0 software. Achieving 90% power at a two-tailed Bonferroni adjusted α of 0.05/3 = 0.017, the calculated number of cases in the control group, the TPVB group, and the ICNB group was 22, 43, and 43 allowing for a 20% loss to follow-up.

2.8 Statistically analysis

Statistical analyses were performed by SPSS software, version 19.0 (SPSS Inc, Chicago, IL). Statistical significance was set at the 5% level. Data distribution was examined by Kolmogorov–Smirnov test. Quantitative data were reported as mean ± SD or median ± inter-quartile range, and categorical data as percentage. Analysis of variance (ANOVA) and Kruskal–Wallis ANOVA were used for evaluating group effects across three groups for means and medians. Post hoc comparison was conducted at an adjusted significance level of 0.05/3 = 0.017. Fisher's exact test was employed for categorical variables.

3 Results

A total of 169 patients were assessed for eligibility for the study, but 41 cases were excluded due to given reasons in Figure 1, and 128 patients were included in the final analysis. Comparable demographic characteristics at baseline were observed among three groups (Table 1).

As shown in Table 2, there was a significant decrease in HZ-BOI-AUC_{30} scores between both the TPVB and ICNB groups, as opposed to the control group. However, no significant difference was found between the TPVB and ICNB groups. More specifically, the mean was 152.2 (95% confidence interval [CI]: 124.7, 179.7), 94.7 (95% CI: 81.5, 107.8), and 111.9 (95% CI: 97.4, 126.4) in control, TPVB, and ICNB groups, respectively. The mean of BOI-AUC_{90} and BOI-AUC_{180} were comparable between the TPVB and ICNB groups, while they were significantly lower than those of the control group. The percentage of cases using rescue analgetic was lower in the TPVB and ICNB groups than in the control group, but the difference was statistically significant only at D30 between the two intervention groups (celecoxib: 39.9 vs 11.0 vs 14.0%, $p < 0.001$ at D30; 26.1 vs 9.6 vs 10.3%, $p = 0.037$ at D90; 20.3 vs 4.4 vs 8.1%, $p = 0.013$ at D180 and oxycodone and acetaminophen: 22.2 vs 9.6 vs 12.5%, $p = 0.202$ at D30; 17.0 vs 5.9 vs 7.4%, $p = 0.039$ at D90; 10.5 vs 2.2 vs 2.9%, $p = 0.032$ at D180, Figure 3).

Compared with the control group, the incidence of PHN, across all follow-up time points, was significantly lower in the TPVB and ICNB groups. However, we found no differences at D90 and D180 between the two intervention groups with respect to PHN incidence (45.4 vs 18.6 vs 20.9%, $p = 0.044$ at D90 and 36.4 vs 9.3 vs 14.0%, $p = 0.018$ at D180) (Table 3).

Compared with baseline HR-QoL scores, patients exhibited a greater improvement among the three groups after 30, 90, and 180 days. However, the effects at D30, 90, and 180 were significantly more apparent in the two intervention groups. Differences between the TPVB and ICNB groups were not significant at D30 or at other follow-up time points. According to EuroQoL 5-Dimension questionnaire (EQ-5D-3L), the proportion of patients who reported significant improvements in terms of pain/discomfort ($p < 0.001$ at D30, $p = 0.017$ at D90, $p < 0.001$ at D180), usual activities ($p < 0.001$ at D30, $p < 0.001$ at D90, $p = 0.025$ at D180), mobility ($p = 0.029$ at D30, $p = 0.042$ at D90, $p < 0.001$ at D180), symptom of anxiety/depression ($p = 0.037$ at D30, $p < 0.001$ at D90, $p < 0.001$ at D180), and self-care ($p = 0.163$ at D30, $p = 0.210$ at D90, $p < 0.001$ at D180) were significantly lower two

Table 1: Baseline characteristics of participants in three groups

Variables	Control group ($N = 26$)	TPVB group ($N = 49$)	ICNB group ($N = 53$)	F/χ^2	p
Age (years)	64.15 ± 8.38	65.49 ± 8.06	66.10 ± 7.53	0.470	0.628
Female sex, *n* (%)	12 (46.2%)	26 (53.1%)	23 (43.4%)	0.983	0.612
Prodromal duration (days)	11.70 ± 1.26	10.90 ± 1.33	10.65 ± 1.50	0.840	0.437
ZBPI: baseline average pain score	8 (4, 10)	8 (6, 10)	8 (7, 10)	0.779	0.677
Distribution of pain, *n* (%)				2.239	0.692
Single thoracic dermatomal	16 (55.2%)	33 (67.3%)	29 (54.7%)		
2–3 thoracic dermatomal	9 (31.0%)	11 (22.4%)	15 (28.3%)		
≥4 thoracic dermatomal	4 (13.8%)	5 (10.2%)	9 (17.0%)		
Affected side, *n* (%)				1.113	0.573
Left	15 (57.7%)	22 (44.9%)	26 (49.1%)		
Right	11 (42.3%)	27 (55.1%)	27 (50.9%)		
Rash severity, *n* (%)				0.956	0.620
Number of lesions <50	18 (69.2%)	37 (75.5%)	42 (79.2%)		
Number of lesions ≥50	8 (30.8%)	12 (24.5%)	11 (20.8%)		
Haemorrhagic lesion, *n* (%)	2 (7.7%)	6 (12.2%)	5 (9.4%)	0.438	0.804
Concomitant disease, *n* (%)					
Hypertension	11 (42.3%)	18 (36.7%)	16 (30.2%)	1.211	0.546
Diabetes mellitus	6 (23.1%)	14 (28.6%)	17 (32.1%)	0.692	0.708
History of previous analgesic use, *n* (%)				1.441	0.837
None	3 (11.1%)	5 (10.2%)	8 (15.1%)		
NSAID	16 (59.3%)	30 (61.2%)	34 (64.2%)		
Anti-epileptic or week opioid	8 (29.6%)	14 (28.6%)	11 (20.8%)		

ZBPI = zoster brief pain inventory; TPVB = thoracic paravertebral block; ICNB = intercostal nerve block; NSAID = non-steroidal anti-inflammatory drugs.

Table 2: HZ-BOI scores of three groups during study days 0–30, 30–90, and 90–180

Group	$BOI\text{-}30_{AUC}$				$BOI\text{-}30\text{-}90_{AUC}$				$BOI\text{-}90\text{-}180_{AUC}$			
	M	**95%CI**	***F***	***p***	***M***	**95%CI**	***F***	***p***	***M***	**95%CI**	***F***	***p***
Control (*n* = 26)	152.2	124.7, 179.7	9.052	<0.001	129.5	106.1, 152.9	10.704	<0.001	117.9	96.5, 139.2	24.062	<0.001
TPVB (*n* = 49)	94.7	81.5, 107.8			82.3	69.1, 95.4			57.9	50.8, 65.0		
ICNB (*n* = 53)	111.9	97.4, 126.4			79.9	70.1, 89.7			62.6	52.6, 72.6		
Post-hot analysis	**MD**	**95%CI**	***p***		**MD**	**95%CI**	***p***		**MD**	**95%CI**	***p***	
Control vs TPVB	57.5	30.8, 84.3	<0.001		47.3	25.1, 69.4	<0.001		59.9	41.8, 78.1	<0.001	
Control vs ICNB	40.3	14.3, 66.2	0.003		49.6	26.7, 72.4	<0.001		55.3	37.6, 72.9	<0.001	
TPVB vs ICNB	17.3	−3.4, 38.0	0.101		2.3	−15.4, 20.0	0.795		4.7	−9.3, 18.8	0.507	

TPVB = thoracic paravertebral block; ICNB = intercostal nerve block; HZ = herpes zoster; BOI = burden of illness; AUC = area under the curve; CI = confidence interval; *M* = mean; MD = mean difference.

intervention groups when compared to the control group at D30, D90, and D180, respectively (Figure 4).

There were no serious adverse events in the present study. There was no serious intravascular injection in either the TPVB or ICNB group. 11.6 and 7.0% of patients experienced dizziness in the TPVB and ICNB group within post-procedural 15 min, respectively. However, the difference was not statistically significant ($p = 0.713$). The incidence of cases complaining of insufferable pain during puncture in the TPVB group was significantly higher than that in the ICNB group (67.4 vs 23.3%, $p < 0.001$). Moreover, the ICNB approach was also associated with significantly shorter procedure time as compared to the conventional TPVB (16.47 ± 3.39 vs 11.69 ± 2.58, $p < 0.001$).

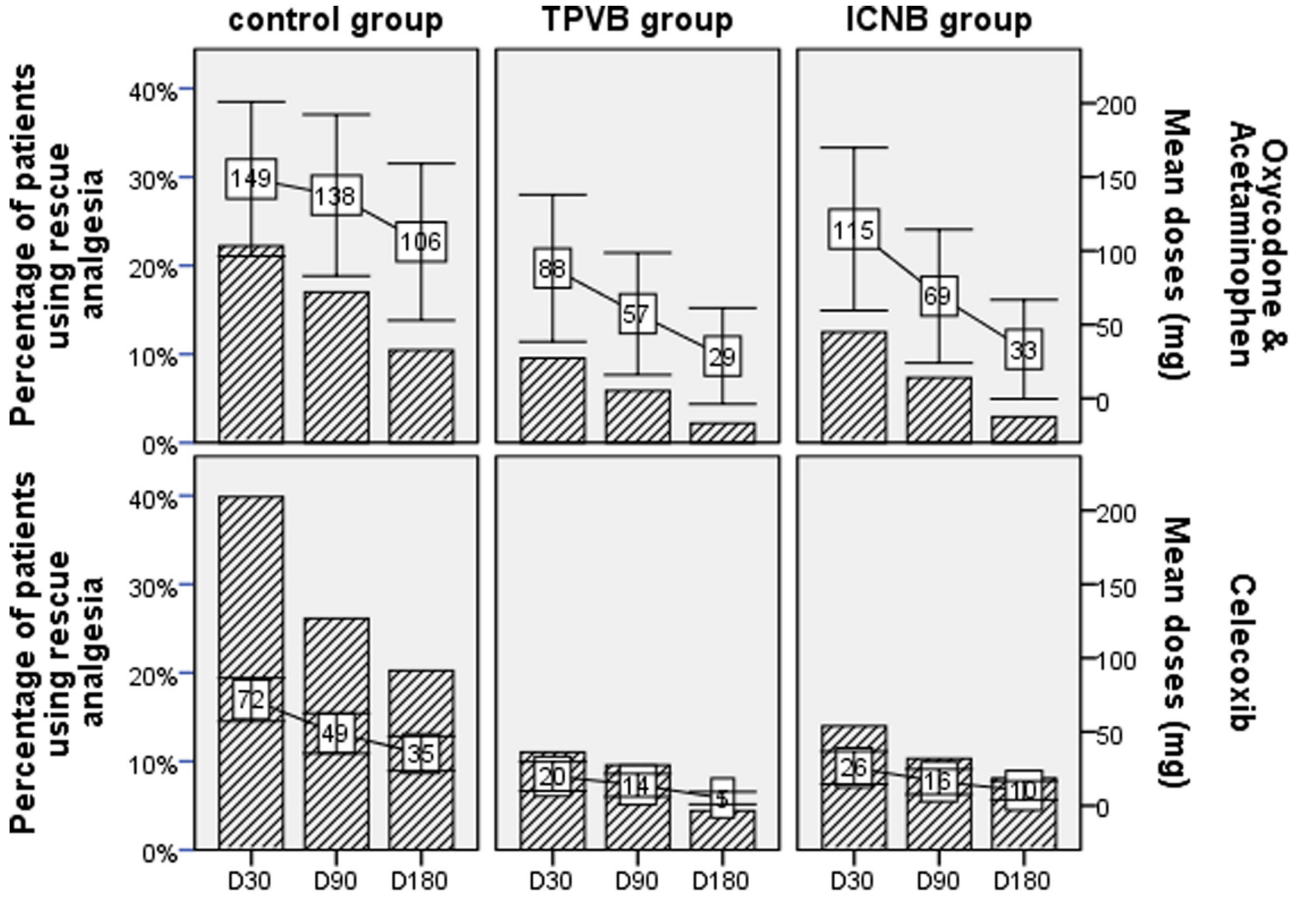

Figure 3: Consumption of rescue analgesics in patients experiencing pain that may not be sufficiently controlled during the follow-up period.

Table 3: PHN incidence for three groups

Content		Post hoc analysis		Difference in incidence (95% CI)	Rate ratio (95% CI)	χ^2 value	*p*
PHN incidence at D90	Control vs TPVB	11/26 (42.3%)	9/49 (18.4%)	23.9% (2.1%, 45.8%)	3.259 (1.127, 9.428)	4.979	0.032
	Control vs ICNB	11/26 (42.3%)	11/53 (20.8%)	21.6% (−0.4%, 43.5%)	2.800 (1.007, 4.070)	4.033	0.045
	TPVB vs ICNB	9/49 (18.4%)	11/53 (20.8%)	−2.4% (−17.8%, 13.0%)	0.859 (0.322, 2.293)	0.092	0.807
PHN incidence at D180	Control vs TPVB	8/26 (30.8%)	4/49 (8.2%)	22.6% (3.3%, 41.9%)	5.000 (1.337, 18.695)	6.459	0.019
	Control vs ICNB	8/26 (30.8%)	6/53 (9.4%)	19.4% (−0.2%, 39.1%)	4.267 (1.233, 14.770)	5.775	0.024
	TPVB vs ICNB	4/49 (8.2%)	6/53 (9.4%)	−3.2% (−14.6%, 8.3%)	0.853 (0.215, 3.379)	0.051	0.821

TPVB = thoracic paravertebral block; ICNB = intercostal nerve block; PHN = post-herpetic neuralgia; D30 = 1 month after recruitment; D90 = 3 months after recruitment; D180 = 6 months after recruitment.

4 Discussion

The findings of this retrospective study showed that US-guided repetitive ICNBs in acute thoracic HZ not only decreased illness burden over 30, 90, and 180 days but also reduced the incidence of PHN at D90 and D180 as effectively as thoracic PVB technique, whereas more effectively than standard AVT. In addition, the ICNB approach was more accessible than the conventional PVB.

Usually, AVT is recommended within 72 h at the initial diagnosis of HZ. A considerable amount of evidence has demonstrated that although antiviral agents and rescue analgesics as the current standard treatment for acute HZ can accelerate healing of the lesions and reduce acute pain, no effect in preventing PHN was observed [15]. During the acute phase of HZ, the reactive VZV replicates and transports from the dorsal root ganglion to the peripheral nerve leading to an inflammation of sensory ganglion and adjacent nerve as well as tissue damage, which mainly accounts for ZAP. Continuous infiltration of inflammatory results in abnormal expression of ion channels, consequent promoted release of neuro-transmitters, and up-regulated nociceptor excitability that leads to central sensitization and makes the disease course persistent [16]. Whereas, once the most common and often difficult-to-cure complication of PHN develops, it not only decreases the HR-QoL in patients but also significantly increases the health burden at both the individual and societal levels. As a result, several supplement interventional procedures have been tried according to the hypothesis that inhibition of inflammatory process and sustained peripheral stimuli reaching the central nervous system throughout the acute phase may alleviate central sensitization and lower the occurrence of PHN, especially for those with risk factors, including older age and greater severity of the prodrome, rash, and ZAP [17]. Literature has shown that the administration of epidural corticosteroid is associated with a reduced PLA_2 activity level within injured nerves to produce a direct anti-inflammation effect by preventing prostaglandin generation. Besides an anti-inflammation action, corticosteroid has the ability to stabilize neural membranes, thus suppressing ectopic neuroma discharges with nerve injury to decrease nociceptive input. Local anesthetic (LA) may offer a therapeutic effect by improving intra-radicular blood flow to reduce neural dysfunction [18–20]. Therefore, an early recognition and prompt management of ZAP with interventional treatment should be emphasized with the possible prevention of PHN.

Neuraxial and sympathetic administration of LA and corticosteroid including intrathecal, epidural, and sympathetic blocks have been reported for the treatment of acute

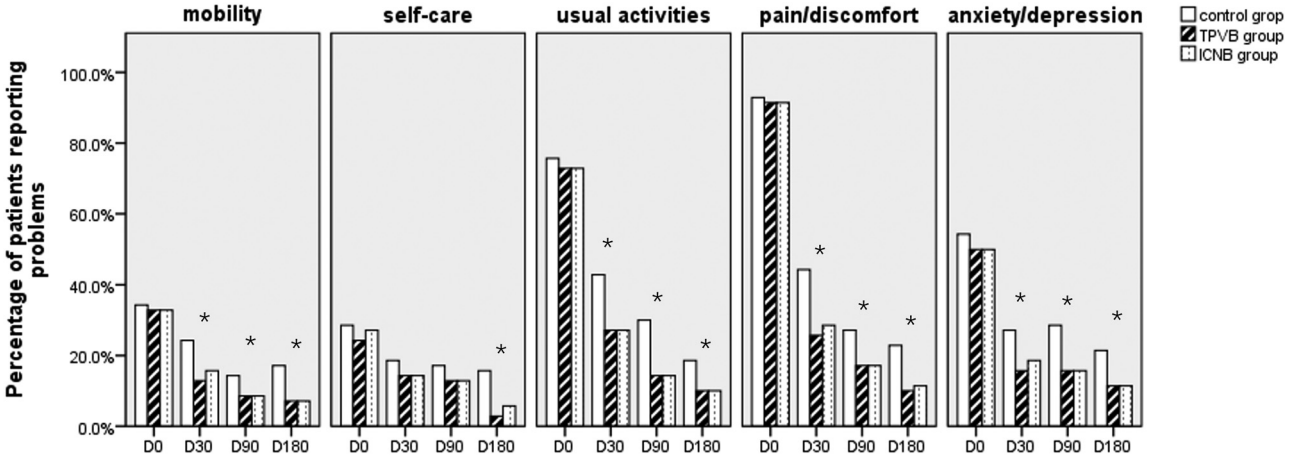

Figure 4: The percentage of patients who reported problems in the five domains of EuroQol EQ-5D at the time of Days 0, 30, 90, and 180. *$p < 0.05$ when compared to the control group.

HZ and PHN. Although the beneficial effect appears to be consistent, this can be challenging when a neuraxial blockade is performed in the thoracic region consequent from the risk of serious complications including hemodynamic instability, spinal hematoma, urinary retention intractable headaches, as well as contraindicated conditions such as coagulopathy [21]. Conversely, the PVB is one of the most commonly used interventions for reducing pain associated with acute HZ. The PVS accommodates LA plus steroid spreading into cephalad, caudal, intercostal, interpleural, epidural, and prevertebral spaces to generate unilateral spinal nerve, together with the rami communicants, the dorsal ramus, and the sympathetic chain [22]. Serious adverse events associated with PVB are relatively rare, but they can lead to the most common development of inadvertent vascular puncture, followed by hypotension, haematoma, pleural puncture, and pneumothorax [23]. In recent years, US guidance is a standard nerve localization technique for peripheral never block allowing visualization of muscles, fascia, target nerve, needle, and LA injectate without contrast agent [24]. Theoretically, the application of US technique to PVB can obtain direct visualization of the entire needle to reduce the risk of adverse effects, while simultaneously confirming proper LA injection with anterior displacement of pleura. Therefore, US-guided PVB generally has a high success rate with few adverse effects [25]. Liu et al. estimated the efficacy of US-guided PVB intervention for the treatment of HZ-related pain with different courses [5]. They found that the best efficacy was achieved in the acute group. Several randomized controlled studies confirmed that lower BOI scores caused by acute pain and PHN during the entire 6-month follow-up were obtained after receiving US-guided repetitive thoracic PVB during the acute phase as opposed to the standard AVT [6,7]. The results are consistent with ours in that the early use of repetitive TPVBs under US guidance was more effective than antivirals alone in reducing HZ-related BOI and improving quality of life at 30, 90, and 180 days post-procedurally. On the basis of our experience, this technique remains the preferred strategy for inhibiting inflammation, facilitating nerve healing, and suppressing the development of PHN, because a lower occurrence of PHN was observed at D90 and D180 post-therapy according to our result.

Considering that the risk of intravascular puncture and pneumothorax increased by repeated injection even under US guidance, as well as the injury tendency due to deeply located targeted nerve structure in thoracic PVB technique, we estimated the ability of a more lateral approach, the ICNB, in terms of assuring efficacy and decreasing complications in the current study. With the addition of US guidance, ICNB has been clinically employed alternative to PVB to provide effective analgesia in a variety of cases including mastectomy, cardiac, thoracic, and abdominal surgery [26]. According to the anatomy, the intercostal space between the adjacent ribs is usually shallower and wider than that between the two thoracic TPs. Therefore, it allows a less steep needle angle trajectory and consequently results in better visualization of needle puncture under real-time guidance. In addition, this block technique can also reduce the risk of inadvertent neuraxial block and hematoma due to the more lateral approach as compared to the conventional PVB [27]. In accordance with what was expected, patients in the ICNB group showed a comparable less illness burden associated with HZ at all time points during the follow-up period, when compared to the TPVB group. A significantly lower incidence of PHN at D90 and D180 was also observed in the ICNB group as compared to the control group. However, no significant

difference was observed between the two procedural groups. Consequently, the same better trend of improved HR-QoL scores during the follow-up period was observed in the ICNB and TPVB groups as opposed to the control group. Importantly, shorter procedure time with lower pain scores during puncture was observed in cases receiving ICNB, which demonstrated that US-guided ICNB was an easier and time-efficient approach than the conventional TPVB. These findings were consistent with that of a previous comparative study, in which the results showed comparable data without significant differences in the pain reduction, duration of HZ treatment, and frequency of injection in both US-guided ICNB and the fluoroscopy (FL)-guided epidural nerve block. However, the ICNB is more accessible than the epidural block under FL guidance, which was recommended as an alternative option for thoracic HZ [9]. Increasing evidence shows that perforation of pleura was one of the most serious complications of TPVB technique, however, no serious advents were observed in the study. This would benefit from the measurement of pleura depth from the entry point before puncture and the real-time guidance during puncture using ultrasonography.

The study did have some limitations. First, although increasing evidence supported the use of US guidance technique in peripheral nerve block, we had to admit that this technique highly depends on the experience of the operator. Second, patients were allowed to use rescue analgesics in this study, which would be a confounding factor in the analysis of the efficacy. Third, the incidence of serious adverse events including advertent vascular puncture and pneumothorax was not significantly different between the two intervention groups, which might be due to the limited sample size, therefore, a well-designed randomized study with a large sample to investigate the safety of US-guided ICNB technique in acute HZ was needed.

In conclusion, our results indicated that both US-guided repetitive ICNB and TPVB were the same effective in patients suffering from thoracic HZ during the acute phase and accounted for the possible prevention of PHN. Additionally, the ICNB under US guidance was an easier and time-efficient approach as opposed to the conventional TPVB technique, which plus the antiviral medications might be encouraged as the established means of preventing the development of PHN after acute thoracic rash presence.

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Research ethics: All methods were carried out in accordance with the principles of the Declaration of Helsinki. The protocol of the study was approved by the institutional Clinical Research Ethics Committee (2023-015KY)s and registered in the Chinese Registry of Clinical Trials (ChiCTR2300076442).

Informed consent: Written informed consent was obtained from all participants before enrollment. The retrospective study was registered in the Chinese Registry of Clinical Trials (ChiCTR2300076442).

Author contributions: The authors have accepted responsibility for the entire content of this manuscript and approved its submission. Runqiao Fu was involved in the conception and design, analysis, and interpretation of the data; the drafting of the paper and revising it critically for intellectual content; and the final approval of the version to be published. Mianrong Xue was involved in the conception and design, analysis, and interpretation of the data; the drafting of the paper; and revising it critically for intellectual content. Rong Yuan was involved in the conception and design, analysis, and interpretation of the data; the drafting of the paper and revising it critically for intellectual content. Yanwei Yang was involved in the conception and design, analysis, and interpretation of the data; the drafting of the paper and revising it critically for intellectual content. Zhenlong Qin was involved in the conception and design and interpretation of the data; the drafting of the paper and revising it critically for intellectual content; and the final approval of the version to be published.

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References

[1] Schmader K. Herpes zoster. Ann Intern Med. 2018;169(3):C19–31.
[2] John AR, Canaday DH. Herpes zoster in the older adult. Infect Dis Clin N Am. 2017;31(4):811–26.
[3] Yawn BP, Saddier P, Wollan PC, St Sauver JL, Kurland MJ, Sy LS. A population-based study of the incidence and complication rates of herpes zoster before zoster vaccine introduction. Mayo Clin Proc. 2007;82(11):1341–9.
[4] Kumar V, Krone K, Mathieu A. Neuraxial and sympathetic blocks in herpes zoster and postherpetic neuralgia: an appraisal of current evidence. Region Anesth Pain Med. 2004;29(5):454–61.

[5] Liu F, Lu GJ, Bai ZY. Efficacy of repetitive paravertebral block combined with medication in the treatment of zoster-related pain with different courses. Neurosciences. 2021;26(2):192–8.
[6] Ma Y, Li B, Sun L, He X, Wu S, Shi F, et al. A prospective randomized comparison of the efficacy of standard antiviral therapy versus ultrasound-guided thoracic paravertebral block for acute herpes zoster. Ann Med. 2022;54(1):369–78.
[7] Deng A, Chen Z, Lin S, Zhou Y, He L. Ultrasound-guided thoracic paravertebral block using paraventricular oblique sagittal (POS) approach for the treatment of acute herpes zoster: A two-blind randomized controlled trial. Pain Ther. 2023;12(3):797–809.
[8] Lopez-Rincon RM, Kumar V. Ultrasound-guided intercostal nerve block. StatPearls Publishing LLC; 2023.
[9] Lee HJ, Park HS, Moon HI, Yoon SY. Effect of ultrasound-guided intercostal nerve block versus fluoroscopy-guided epidural nerve block in patients with thoracic herpes zoster: A comparative study. J Ultras Med. 2019;38(3):725–31.
[10] von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg. 2014;12(12):1495–9.
[11] Coplan PM, Schmader K, Nikas A, Chan IS, Choo P, Levin MJ, et al. Development of a measure of the burden of pain due to herpes zoster and postherpetic neuralgia for prevention trials: adaptation of the brief pain inventory. J Pain. 2004;5(6):344–56.
[12] Callegaro A, Curran D, Matthews S. Burden-of-illness vaccine efficacy. Pharm Stat. 2020;19(5):636–45.
[13] Hurst NP, Kind P, Ruta D, Hunter M, Stubbings A. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). Br J Rheumatol. 1997;36(5):551–9.
[14] Kim HJ, Ahn HS, Lee JY, Choi SS, Cheong YS, Kwon K, et al. Effects of applying nerve blocks to prevent postherpetic neuralgia in patients with acute herpes zoster: A systematic review and meta-analysis. Korean J Pain. 2017;30(1):3–17.
[15] Chen N, Li Q, Yang J, Zhou M, Zhou D, He L. Antiviral treatment for preventing postherpetic neuralgia. Cochrane Database Syst Rev. 2014;2014(2):D6866.
[16] Wu CL, Marsh A, Dworkin RH. The role of sympathetic nerve blocks in herpes zoster and postherpetic neuralgia. Pain. 2000;87(2):121–9.
[17] Zhou H, Wang Z, Jin H, Chen X, Lei L. A systematic review and meta-analysis of independent risk factors for postherpetic neuralgia. Ann Palliat Med. 2021;10(12):12181–9.
[18] Yabuki S, Kikuchi S. Nerve root infiltration and sympathetic block. An experimental study of intraradicular blood flow. Spine. 1995;20(8):901–6.
[19] Devor M, Govrin-Lippmann R, Raber P. Corticosteroids suppress ectopic neural discharge originating in experimental neuromas. Pain. 1985;22(2):127–37.
[20] Flower RJ, Blackwell GJ. Anti-inflammatory steroids induce biosynthesis of a phospholipase A2 inhibitor which prevents prostaglandin generation. Nature. 1979;278(5703):456–9.
[21] McGrath JM, Schaefer MP, Malkamaki DM. Incidence and characteristics of complications from epidural steroid injections. Pain Med. 2011;12(5):726–31.
[22] Ardon AE, Lee J, Franco CD, Riutort KT, Greengrass RA. Paravertebral block: Anatomy and relevant safety issues. Korean J Anesthesiol. 2020;73(5):394–400.
[23] Naja Z, Lonnqvist PA. Somatic paravertebral nerve blockade. Incidence of failed block and complications. Anaesthesia. 2001;56(12):1184–8.
[24] Helen L, O'Donnell BD, Moore E. Nerve localization techniques for peripheral nerve block and possible future directions. Acta Anaesth Scand. 2015;59(8):962–74.
[25] Krediet AC, Moayeri N, van Geffen GJ, Bruhn J, Renes S, Bigeleisen PE, et al. Different approaches to ultrasound-guided thoracic paravertebral block: An illustrated review. Anesthesiology. 2015;123(2):459–74.
[26] Szamborski M, Janc J, Rosinczuk J, Janc JJ, Lesnik P, Lysenko L. Use of ultrasound-guided interfascial plane blocks in anterior and lateral thoracic wall region as safe method for patient anesthesia and analgesia: Review of techniques and approaches during COVID-19 pandemic. Int J Environ Res Public Health. 2022;19(14):8696.
[27] Vlassakov K, Vafai A, Ende D, Patton ME, Kapoor S, Chowdhury A, et al. A prospective, randomized comparison of ultrasonographic visualization of proximal intercostal block vs paravertebral block. BMC Anesthesiol. 2020;20(1):13.