KJP

Korean J Pain 2024;37(4):343-353
https://doi.org/10.3344/kjp.24111
pISSN 2005-9159, eISSN 2093-0569

Clinical Research Article

Assessment of ultrasound-guided intercostal nerve block for acute herpes zoster and its' possible prophylaxis for postherpetic neuralgia: a retrospective and case-controlled trial

Xiuhua Li[1], Rong Yuan[2], Yanwei Yang[3], Zhenlong Qin[4], and Runqiao Fu[5]

[1]Department of Anesthesiology, Capital Medical University Affiliated Beijing Tongren Hospital, Beijing, China
[2]Department of Ultrasonic Diagnosis, North Distirct of Peking University Third Hospital, Peking University, Beijing, China
[3]Department of Anesthesiology, Beijing Chuiyangliu Hosptial, Beijing, China
[4]Department of Anesthesiology, Dongfang Hospital Beijing University of Chinese Medicine, Beijing, China
[5]Department of Anesthesiology, Beijing Chuiyangliu Hosptial Affiliated to Tsinghua University, Beijing, China

ABSTRACT

Background: This study aimed to compare the intercostal nerve block (ICNB) and thoracic paravertebral block (TPVB) for acute herpes zoster-associated pain (ZAP) and possible prophylaxis for post-herpetic neuralgia (PHN).
Methods: This study enrolled 128 patients with ZAP. Their records were stratified into standard antiviral treatment (AVT) plus US-guided TPVB (the TPVB group), AVT plus US-guided ICNB (the ICNB group) or AVT alone (the control group). Herpes zoster (HZ)-related burden of illness (HZ-BOI) within the post-procedural 30 days was defined as the primary endpoint, determined by a composite of pain severity and follow-up duration. Procedure time, rescue analgesic requirement, PHN incidence, health-related quality of life and side effects were also recorded.
Results: Significantly lower HZ-BOI-AUC$_{30}$ was reported in the TPVB and ICNB groups as compared to the control group, with a mean difference of 57.5 (P < 0.001) and 40.3 (P = 0.003), respectively. However, there was no difference between the TPVB and ICNB groups (P = 0.978). Both TPVB and ICNB reported significantly greater improvements in PHN incidence, EQ-5D-3L scores and rescue analgesic requirements during follow-up, as opposed to the control AVT. Shorter procedure time was observed in ICNB as compared to TPVB (16.47 ± 3.39 *vs*. 11.69 ± 2.58, P < 0.001).
Conclusions: Both US-guided TPVBs and ICNBs were effective for ZAP, and accounted for possible prophylaxis for PHN, as compared to AVT alone. The ICNB approach could be recommended as an alternative to conventional TPVB with a better consumed procedure time and side effect profile.

Keywords: Herpes Zoster; Intercostal Nerves; Nerve Block; Postherpetic Neuralgia; Ultrasonography.

Received April 8, 2024; Revised July 31, 2024; Accepted August 5, 2024

Handling Editor: Seong-Soo Choi

Correspondence: Runqiao Fu
Department of Anesthesiology, Beijing Chuiyangliu Hosptial Affiliated to Tsinghua University, No. 2 Chuiyangliu Street, Chaoyang District, Beijing 100021, China
Tel: +86-13501190076, Fax: +86-010-67700631, E-mail: furqanesthesiapain@163.com

Zhenlong Qin
Department of Anesthesiology, Dongfang Hospital Beijing University of Chinese Medicine, No. 6 fangxingyuan Fengtai District, Beijing 100078, China
Tel: +86-13581804165, Fax: +86-010-67689652, E-mail: qinzlanesthesia@163.com

INTRODUCTION

Herpes zoster (HZ) usually presents as a unilateral band-like vesicular rash in the dermatome corresponding to the affected nerve caused by a reactivation of varicella zoster viruses (VZV) latent in the sensory ganglion [1]. The crude prevalence of HZ in the general population is from 20% to 30%, with an increasing incidence over 50 years of age, with an approximate occurrence of 50% in those aged 85 years [2]. During the acute episode, the treatment is focused on decreasing the intensity and duration of symptom and preventing complications. Postherpetic neuralgia (PHN), defined as acute zoster associated pain (ZAP) sustained for at least 90 days after the rash, is a debilitating complication of HZ. PHN becomes more common with increasing age, affecting about 5% of those younger than 60 years, increasing to 20% of those 80 years and older, according to a large population-based study [3]. Unfortunately, there is still no reliable intervention that relieves the pain of PHN [4]. Therefore, effective treatments to prevent PHN have become an important focal point in current research. Epidemiological research reported that interventions aimed at reducing the inflammation and repetitive painful stimuli during acute zoster might attenuate central sensitization, and consequently reduce the prevalence of PHN [5]. In this respect, ultrasound (US)-guided paravertebral block (PVB) is effective in resolving pain in acute HZ and appears capable of preventing the incidence of PHN [6–8]. Compared with 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 for rib fractures [9]. However, to the authors' knowledge, there was only one comparative trial with a small sample, estimating the effect of ICNB for acute HZ [10]. Therefore, it was hypothesized that the application of repetitive ICNBs technique under US guidance during the acute phase of HZ could significantly reduce the HZ-related burden of illness (HZ-BOI) over 30 days (HZ-BOI-AUC_{30} scores). It might be an alternative to the conventional thoracic paravertebral blocks (TPVBs) in providing acute pain management and possible prophylaxis for PHN in patients with thoracic HZ. Furthermore, it was a more time-efficient approach and had a better side effect profile compared to TPVB.

MATERIALS AND METHODS

1. Study design

This present study was conducted as a case-control retrospective trial in accordance with the principles of the Declaration of Helsinki and the guidelines of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) [11]. The protocol 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 visited the pain clinic in the anesthesiology department for the treatment of thoracic herpetic eruption were reviewed and divided into groups according to the treatment they received, which mainly depended on patients' choices after clinicians provided the estimates of the strength and benefits of three treatment modalities (**Fig. 1**). These groups included a control group, which received antiviral treatment (AVT) for a standard 7-day course (valacyclovir 0.3 g, three times daily) immediately after enrollment; the TPVB group, which received the same AVT as well as US-guided repeated TPVB injections following AVT; and the ICNB group, which received the AVT plus the subsequent US-guided repeated ICNB. Injection was repeated every 48 hours for a week up to 4 times. Celecoxib (200 mg tablets, up to 2 times daily) as well as oxycodone & acetaminophen (5 mg:325 mg tablets, up to 4 times daily) were respectively offered as rescue analgesics according to pain intensity following the guidelines of World Health Organization [12]. On the other hand, antidepressant or antiepileptic drugs and other nerve blocks, including epidural or intrathecal blocks, were prohibited.

2. Participants

The inclusion criteria were as follows: (1) HZ-related acute pain originating from thoracic dermatome; (2) less than a 4-week duration from initial rash onset; (3) moderate to severe pain according to numeric rating scale (NRS) scores ≥ 4; and (4) being age 50 years or older. Patients who had immunity impairment, hepatic or renal dysfunction, coagulopathy, cognitive disorders, analgesic addition, pregnancy/lactation, severe skin lesions due to blisters, who were converting to other procedures during the follow-up period, or had incomplete medical data

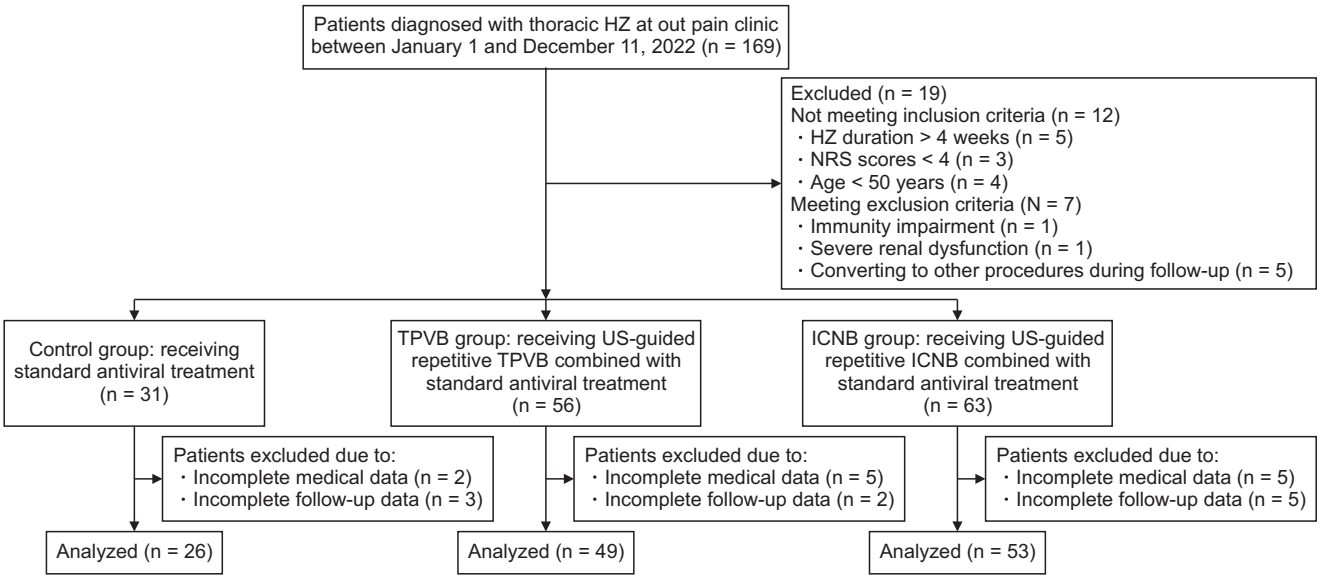

Fig. 1. The diagram of patient recruitment. HZ: herpes zoster, NRS: numeric rating scale, TPVB: thoracic paravertebral block, ICNB: intercostal nerve block, US: ultrasound.

were excluded.

3. Procedures description

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

4. US-guided TPVB procedure

A convex array US probe with a low-frequency (2–5 MHz) transducer was placed in a transverse position parallel to the spinous process at the targeted thoracic spinal segment to achieve a transverse axis view of the vertebral plate and transverse process (TP), which was recognized as a hyper-echoic structure with an anterior dark acoustic shadow. The probe was then slightly moved in the caudal direction until the above-mentioned typical images disappeared. Parts of thoracic paravertebral space (PVS) were visualized in the hyperechoic image comprising the parietal pleura, superior costotransverse ligament, and internal intercostal membrane. After verification that no vulnerable blood vessel was abnormally located on the puncture path using the color Doppler mode, a 22-gauge needle was advanced from the lateral side to the targeted TPVB using an in-plane view (**Fig. 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 dermatome without any adverse events, a single 5 mL mixture comprising 0.5% lidocaine and 5 mg triamcinolone diluted by normal saline was injected using real-time US guidance. Subsequently, the PVS was widened by the anterior displacement of the pleura in the US scan, which confirmed a correct injection.

5. US-guided ICNB procedure

In this technique, the same low-frequency transducer was positioned 6–8 cm lateral from the midline at the targeted intercostal space. Two adjacent ribs were seen as hyperechoic and their characteristic rounded structures were seen in the sagittal US image. An acoustic window was clearly visualized as lying among the intercostal ligaments, the intercostal space, and the parietal pleura between the acoustic shadows of the two ribs. Using Doppler US, the intercostal vessels were readily visible at the lower margin of the upper rib. Additionally, the targeted intercostal nerve root was laying beneath the intercostal arteries (**Fig. 2B**). The same 22-gauge block needle was inserted in-plane caudal-cranial 1 cm away from the transducer under the real-time US beam. The same experimental lidocaine was injected after negative aspiration to confirm anesthesia/pain alleviation in the affected dermatome without any side effects. Success of the block was achieved with the same therapeutic injection using

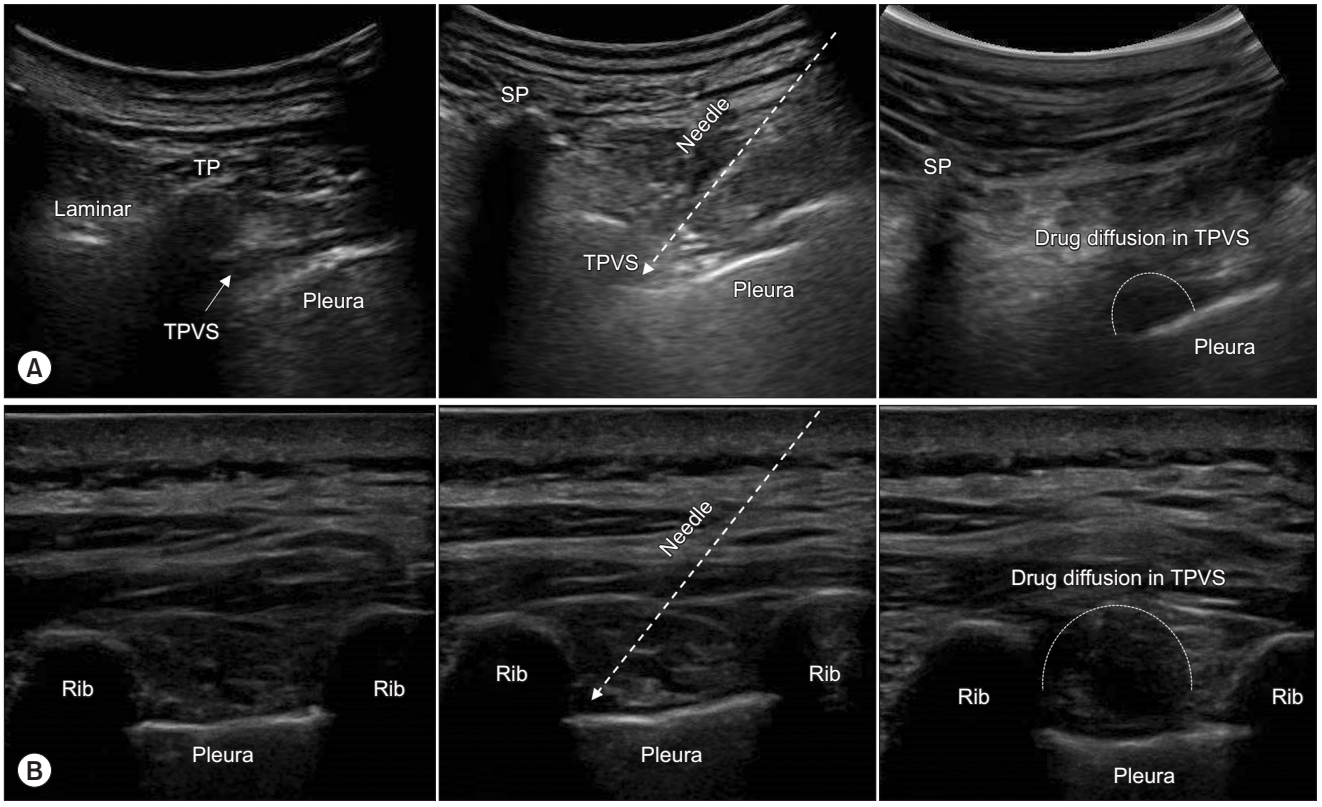

Fig. 2. (A) Thoracic paravertebral block under US guidance. (B) Intercostal nerve block under US guidance. US: ultrasound, TP: transverse process, TPVS: thoracic paravertebral space, SP: spinous process.

0.5% lidocaine, 1 mg/mL triamcinolone, and normal saline in the amount of 5 mL, and subsequent distribution along the intercostal space on the sagittal axis view.

6. Outcome measures and data collection

Pain severity was evaluated using an 11-point scale Likert scale ranging from 0 to 10, which was obtained from Item 3 of the Zoster Brief Pain Inventory (ZBPI) to indicate 'the worst pain during the last 24 hours' [13]. BOI due to HZ was determined by a composite measure of pain severity and HZ disease duration. It was calculated from the area under the curve (AUC) consisting of cumulative ZBPI worst pain scores over the time from the first day of rash onset to the predefined follow-up days using GraphPad Prism version 5.0 (GraphPad Software Inc.) [14]. The Euro-QoL 5-Dimension questionnaire (EQ-5D-3L) was employed to measure the health-related quality of life (HR-QoL), which comprised five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension was divided into one of the three levels: no problems, some problems and extreme problems [15]. PHN was pre-defined as a 'worst' pain score ≥ 3 in the ZBPI, which persisted 90 days after rash onset [16]. The consumption of rescue analgesics and adverse events were also documented.

The primary endpoint was BOI scores due to HZ over 30 days (BOI-AUC_{30}). Follow-ups were conducted every week for the first month at the pain clinic and then in 3-month (D90) intervals for 6 months (D180) *via* telephone by two specially trained nurses who were blinded to the patients' assignment.

7. Sample size calculation

The study derived the efficacy statistic based on BOI-AUC_{30} scores. Based on the previous study, the mean of BOI-AUC_{30} was reported as 110 with a standard deviation (SD) of 20 to 35 by 5 after the antiviral therapy alone [7]. The author wanted to compare the responses of two intervention groups to the control group with a shift of at least a 20% decrease in the mean of BOI-AUC_{30} scores. 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. To obtain a power of 90% with a two-tailed Bonferroni adjusted significance level of 0.05/3

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* value
Age (yr)	64.15 ± 8.38	65.49 ± 8.06	66.10 ± 7.53	0.470	0.628
Female sex	12 (46.2)	26 (53.1)	23 (43.4)	0.983	0.612
Prodromal duration (day)	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				1.978	0.740
Single thoracic dermatomal	16 (55.2)	33 (67.3)	29 (54.7)		
2–3 thoracic dermatomal	7 (26.9)	11 (22.4)	15 (28.3)		
≥ 4 thoracic dermatomal	3 (11.5)	5 (10.2)	9 (17.0)		
Affected side				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				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	2 (7.7)	6 (12.2)	5 (9.4)	0.438	0.804
Concomitant disease					
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				1.551	0.818
None	3 (11.1)	5 (10.2)	8 (15.1)		
NSAID	15 (57.7)	30 (61.2)	34 (64.2)		
Anti-epileptic or week opioid	8 (30.8)	14 (28.6)	11 (20.8)		

Values are presented as number (%) or mean ± standard deviation.
TPVB: thoracic paravertebral block, ICNB: intercostal nerve block, ZBPI: Zoster Brief Pain Inventory, NSAID: non-steroidal anti-inflammatory drugs.

= 0.017, the calculated sample size in the control, TPVB, and ICNB groups was 22, 43, and 43, respectively, allowing for a 20% loss to follow-up.

8. Statistically analysis

SPSS software, version 22.0 (IBM Co.) was used for statistical analyses. Statistical significance was set at the 5% level. Data distribution was examined by the Kolmogorov–Smirnov test. Quantitative data were reported as mean ± SD or median ± inter-quartile range, and categorical data as a percentage. Differences in the change of BOI scores within and across groups were determined using repeated measures analysis of variance, taking treatment as the fixed factor and baseline NRS scores as the covariate. *P* value significance was adjusted for multiple comparisons using the Bonferroni method (0.05/3 = 0.017). Fisher's exact test was employed for categorical variables.

RESULTS

A total of 169 patients were assessed for eligibility, but 41 cases were excluded due to given reasons in **Fig. 1**, hence, 128 patients were included in the final analysis. There were no differences in demographic characteristics at baseline among the three groups (**Table 1**).

As shown in **Table 2**, there was a significant decrease in HZ-BOI-AUC$_{30}$ scores in both the TPVB and ICNB groups, in comparison to the control group. However, no significant difference was found between the TPVB and ICNB groups. More specifically, the mean in the control group was 152.2 (95% confidence interval [CI]: 124.7, 179.7), 94.7 (95% CI: 81.5, 107.8) in TPVB group, and 111.9 (95% CI: 97.4, 126.4) in the control group. 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 analgesics was lower in the TPVB and ICNB groups than the control group, but the difference was statistically significant only at D30 between the two

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* value	M	95% CI	F	*P* value	M	95% CI	F	*P* value
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* value	MD	95% CI		*P* value	MD	95% CI		*P* value
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

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

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 & 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, **Fig. 3**).

Compared with the control group, the incidence of PHN was significantly lower in the TPVB and ICNB groups across all follow-up time points. However, no differences were found 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**).

Patients among the three groups demonstrated a greater improvement in HR-QoL after 30, 90, and 180 days, as compared to their baseline value. 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 the EQ-5D-3L, significant improvements at all time points within the 6-month follow-up period were observed in two intervention groups regarding the domains 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), when compared with the control group (**Fig. 4**).

No serious adverse events were observed in the study. There was no serious intravascular injection in either the TPVB or ICNB group. While 11.6% and 7.0% of cases in the TPVB and ICNB groups experienced dizziness within 15 minutes after injection, respectively, the difference did not reach the level of statistical significance ($P = 0.713$). However, the incidence of patients complaining of insufferable pain during puncture was significantly higher in the TPVB group than in the ICNB group (67.4% *vs*. 23.3%, $P < 0.001$). Moreover, the ICNB approach was also associated with a significantly shorter procedure time as compared to the conventional TPVB (16.47 ± 3.39 *vs*. 11.69 ± 2.58, $P < 0.001$).

DISCUSSION

The findings of this retrospective study illustrated that US-guided repetitive ICNBs for acute thoracic HZ significantly decreased illness burden over 30, 90, and 180 days.

https://doi.org/10.3344/kjp.24111

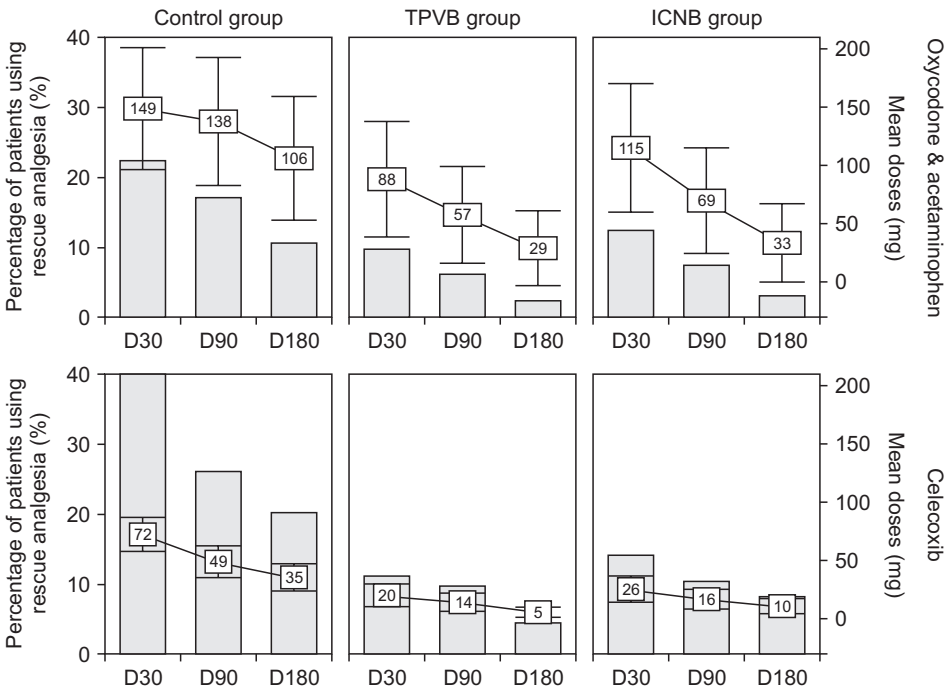

Fig. 3. Consumption of rescue analgesics in patients experiencing pain that may not be sufficiently controlled during the follow-up period. TPVB: thoracic paravertebral block, ICNB: intercostal nerve block.

It was attributable to better analgesia in terms of reduced incidence of PHN, less rescue analgesic consumption, and greater improvements of HR-QoL between ICNB and AVT alone. In addition, the ICNB approach was more time-efficient than the conventional PVB.

Usually, AVT is recommended within 72 hours 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 the healing of lesions and decrease acute pain, nevertheless, high quality evidence showed that oral antiviral drugs do not reduce the incidence of PHN significantly [17]. During the acute phase of HZ, the reactive VZV replicates in the dorsal root ganglion (DRG), and transports to the peripheral nerve leading to an inflammation of the sensory ganglion and adjacent nerve as well as causing tissue damage, which mainly accounts for ZAP. Continuous infiltration of inflammation results in an abnormal expression of ion channels and consequently promoted the release of neuro-transmitters, up-regulated nociceptor excitability that leads to central sensitization, and makes the disease course persistent [18]. Whereas, once the most common and difficult-to-cure complication of PHN develops, it not only decreases HR-QoL in patients but also significantly increases the healthcare burden at both the individual and societal levels. As a result, several supplemental interventional procedures have been tried according to the hypothesis that inhibition of the inflammatory process and sustained peripheral stimuli reaching the central nervous system throughout the acute phase not only alleviate central sensitization but also lower the occurrence of PHN, especially for those with risk factors including older age and greater severity of the prodrome, rash, and ZAP [19]. Studies have shown that the administration of epidural corticosteroids is associated with a reduced PLA_2 activity level within injured nerves to produce a direct anti-inflammation effect by preventing prostaglandin generation. It is also suggested that besides an anti-inflammation action, a corticosteroid was able to stabilize neural membranes, thus suppressing ectopic neural 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 [20–22]. Therefore, early recognition and prompt management of ZAP with interventional treatment should be emphasized for the possible prevention of PHN.

Neuraxial and sympathetic administration of LA and corticosteroids including intrathecal, epidural, and sympathetic blocks have been reported to be effective in controlling pain caused by 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 as a result of the risk of serious complications including instability of hemodynamic, spinal

Table 3. PHN incidence for three groups

Content		*Post-hoc* analysis		Difference in incidence (95% CI)	Rate ratio (95% CI)	χ^2 value	*P* value
PHN incidence at D_{90}	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 D_{180}	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 (11.3%)	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

PHN: post herpetic neuralgia, CI: confidence interval, D_{90}: 3-month after recruitment, D_{180}: 6-month after recruitment, TPVB: thoracic paravertebral block, ICNB: intercostal nerve block.

hematoma, urinary retention, intractable headaches, as well as contraindicated conditions such as coagulopathy [23]. Conversely, the PVB is one of the most common interventions used for managing pain associated with acute HZ. The PVS accommodates LA plus steroid spreading into the cephalad, caudal, intercostal, interpleural, epidural, and prevertebral spaces to generate block effect in the unilateral spinal nerve together with the rami communicants and the dorsal ramus, as well as the sympathetic chain [24]. Although serious PVB-related adverse events are relatively rare, the most commonly occurring are inadvertent vascular puncture, followed by hypotension, haematoma, pleural puncture, and pneumothorax [25]. In recent years, US guidance has been considered a standard localization technique for peripheral nerve block owing to visualization of the muscles, fascia, nerve, needle, and LA injectate without use of a contrast agent [26]. Theoretically, the application of US technique to PVB can capture the direct visualization of the entire needle, while simultaneously confirming proper LA injection with the anterior displacement of the pleura to reduce the risk of adverse effects. Therefore, US-guided PVB is generally associated with a high success rate, with few adverse effects [27]. Liu et al. [6] estimated the efficacy of US-guided PVB intervention for the treatment of ZAP using a different course. They found that the best efficacy was achieved in the acute group. Several randomized controlled studies confirmed that lower BOI caused by acute pain and incidence of 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 [7,8]. These results are consistent with the present study, in that the early use of repetitive thoracic PVB under US guidance was more effective than antiviral medications alone in reducing HZ-related BOI and improving QoL at 30, 90, and 180 days after inclusion, on the basis of the authors' experience, this technique remains the preferred strategy for inhibiting inflammation, facilitating nerve healing and suppressing the development of PHN, because lower occurrence of PHN was observed at D90 and D180 post-therapy according to the present study.

Considering that the risk of intravascular puncture and pneumothorax were increased by repeated injection even under US guidance, as well as the injury tendency due to the deeply located targeted nerve structure in thoracic PVB technique, the authors estimated the efficacy of the ICNB, a more lateral approach, in terms of assuring efficacy and decreasing complications in the current study. On the basis of US guidance, ICNB has been clinically

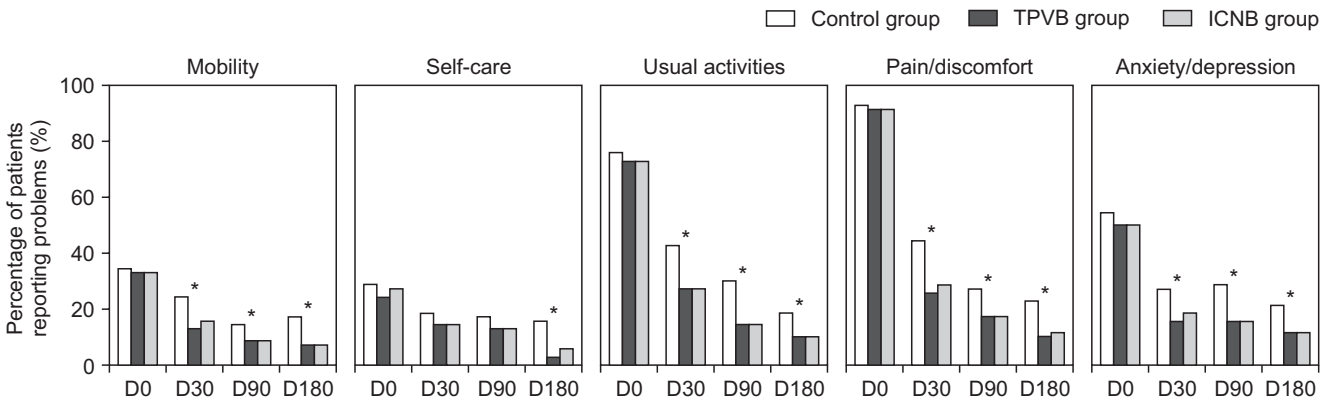

Fig. 4. The percentage of patients who reported problems in the five domains of EuroQol EQ-5D at the time of Day 0, 30, 90 and 180. TPVB: thoracic paravertebral block, ICNB: intercostal nerve block. *$P < 0.05$ when compared to control group.

used as an alternative to PVB to provide effective analgesia in a diversity of cases including mastectomy, cardiac, thoracic, and abdominal surgery [28]. According to the anatomy, the intercostal space between the adjacent ribs is usually shallower and wider than that between the two thoracic TP, which allows a less steep needle angle trajectory and consequently results in a better visualization of the needle puncture under real-time guidance. In addition, this block technique can also reduce the risk of inadvertent neuraxial block and hematoma owing to the more lateral approach as compared to the conventional PVB [29]. In accordance with what was expected, patients in the ICNB group showed less illness burden related to HZ at all time points during the follow-up period as compared to TPVB group. And significantly lower incidence of PHN at D90 and D180 were also observed in the ICNB group as opposed to the control group. There was no significant difference between the two intervention groups. Furthermore, the same better trend in improved QoL during the follow-up period was observed in the ICNB group and TPVB group as opposed to the control group. Importantly, less procedure time with a lower incidence of insufferable pain during puncture was observed in patients receiving ICNB demonstrating that the US-guided ICNB was an easier and more time-efficient approach than the conventional TPVB. However, providing complete pain relief, as perceived by patients during puncture, might be very challenging, especially when the ICNB procedures needs to be repeated. These findings were consistent with that of a previous comparative study, their results showed comparable data in the pain reduction, treatment duration, and injection frequency in both US-guided ICNB and the fluoroscopy (FL)-assisted epidural nerve block. But the ICNB is more accessible than the epidural block under FL guidance, which was recommended as an alternative option for thoracic HZ [30]. Increasing evidence shows that perforation of pleura was one of the most serious complications of TPVB technique, however, no serious adverse events were observed in the study. This would be benefit from the measurement of pleura depth from entry point before puncture and the real-time guidance during puncture using ultrasonography. Nevertheless, unlike the TPVB, ICNB only targets the peripheral branches of the thoracic nerve roots, not the DRG itself, which primarily accounts for ZAP. Consequently, the positive results in comparing the effectiveness of PVB and ICNB in preventing PHN or other second outcomes might be understated due to the sample size being kept small by adopting HZ-BOI as the primary outcome.

The study did have some limitations. Firstly, although increasing evidence supported the use of US guidance technique in the peripheral nerve block, it was necessary to admit that this technique was highly experience dependent. Secondly, patients were allowed to use rescue analgesics in this study, which would be a confounding factor in the analysis of procedural efficacy. Thirdly, incidence of serious adverse events including inadvertent 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 is needed.

In conclusion, both US-guided repetitive TPVBs and ICNBs were effective for acute HZ in thoracic dermatomes as compared to AVT alone, and accounted for the possible prophylaxis for PHN. Additionally, the ICNB approach was a time-efficient approach with a lower risk of side effects as opposed to conventional TPVB technique, which might be encouraged as an alternative to conven-

tional TPVB.

DATA AVAILABILITY

The data are available from the corresponding author, Professor Furan Qiao, upon reasonable request.

ACKNOWLEDGMENTS

The authors would like to thank all subjects for their involvement.

FUNDING

No funding to declare.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Xiuhua Li: Writing/manuscript preparation; Rong Yuan: Methodology; Yanwei Yang: Data curation; Zhenlong Qin: Writing/manuscript preparation; Runqiao Fu: Supervision.

ORCID

Xiuhua Li, https://orcid.org/0000-0002-7117-7968
Rong Yuan, https://orcid.org/0009-0005-6159-8063
Yanwei Yang, https://orcid.org/0009-0001-5546-0579
Zhenlong Qin, https://orcid.org/0009-0000-6096-7449
Runqiao Fu, https://orcid.org/0009-0005-8601-2372

REFERENCES

1. Schmader K. Herpes zoster. Ann Intern Med 2018; 169: ITC19-31. Erratum in: Ann Intern Med 2018; 169: 516.
2. John AR, Canaday DH. Herpes zoster in the older adult. Infect Dis Clin North Am 2017; 31: 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: 1341-9.
4. Nalamachu S, Morley-Forster P. Diagnosing and managing postherpetic neuralgia. Drugs Aging 2012; 29: 863-9.
5. Kumar V, Krone K, Mathieu A. Neuraxial and sympathetic blocks in herpes zoster and postherpetic neuralgia: an appraisal of current evidence. Reg Anesth Pain Med 2004; 29: 454-61.
6. 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 (Riyadh) 2021; 26: 192-8.
7. 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: 369-78.
8. 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: 797-809.
9. Lopez-Rincon RM, Hendrix JM, Kumar V. Ultrasound-guided intercostal nerve block. StatPearls Publishing. 2024.
10. 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 Ultrasound Med 2019; 38: 725-31.
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 2014; 12: 1495-9.
12. Carlson CL. Effectiveness of the World Health Organization cancer pain relief guidelines: an integrative review. J Pain Res 2016; 9: 515-34.
13. 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: 344-56.
14. Callegaro A, Curran D, Matthews S. Burden-of-

illness vaccine efficacy. Pharm Stat 2020; 19: 636-45.
15. 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: 551-9.
16. Curran D, Schmidt-Ott R, Schutter U, Simon J, Anastassopoulou A, Matthews S. Impact of herpes zoster and postherpetic neuralgia on the quality of life of Germans aged 50 or above. BMC Infect Dis 2018; 18: 496.
17. Chen N, Li Q, Yang J, Zhou M, Zhou D, He L. Antiviral treatment for preventing postherpetic neuralgia. Cochrane Database Syst Rev 2014; 2014: CD006866.
18. Wu CL, Marsh A, Dworkin RH. The role of sympathetic nerve blocks in herpes zoster and postherpetic neuralgia. Pain 2000; 87: 121-9.
19. 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: 12181-9.
20. Yabuki S, Kikuchi S. Nerve root infiltration and sympathetic block. An experimental study of intraradicular blood flow. Spine (Phila Pa 1976) 1995; 20: 901-6.
21. Devor M, Govrin-Lippmann R, Raber P. Corticosteroids suppress ectopic neural discharge originating in experimental neuromas. Pain 1985; 22: 127-37.
22. Flower RJ, Blackwell GJ. Anti-inflammatory steroids induce biosynthesis of a phospholipase A2 inhibitor which prevents prostaglandin generation. Nature 1979; 278: 456-9.
23. McGrath JM, Schaefer MP, Malkamaki DM. Incidence and characteristics of complications from epidural steroid injections. Pain Med 2011; 12: 726-31.
24. Ardon AE, Lee J, Franco CD, Riutort KT, Greengrass RA. Paravertebral block: anatomy and relevant safety issues. Korean J Anesthesiol 2020; 73: 394-400.
25. Naja Z, Lönnqvist PA. Somatic paravertebral nerve blockade. Incidence of failed block and complications. Anaesthesia 2001; 56: 1184-8.
26. Helen L, O'Donnell BD, Moore E. Nerve localization techniques for peripheral nerve block and possible future directions. Acta Anaesthesiol Scand 2015; 59: 962-74.
27. 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: 459-74.
28. Szamborski M, Janc J, Rosińczuk J, Janc JJ, Leśnik P, Łysenko 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: 8696.
29. 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: 13.
30. Guerra-Londono CE, Privorotskiy A, Cozowicz C, Hicklen RS, Memtsoudis SG, Mariano ER, et al. Assessment of intercostal nerve block analgesia for thoracic surgery: a systematic review and meta-analysis. JAMA Netw Open 2021; 4: e2133394.