Randomized Trial

A Prospective, Randomized Cross-Over Trial of T2 Paravertebral Block as a Sympathetic Block in Complex Regional Pain Syndrome

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Background: Sympathetic block is commonly performed in clinical practice for management of intractable pain conditions. However, stellate ganglion block (SGB) alone often does not achieve sufficient sympatholysis of the upper extremity. The paravertebral space continues up to the cervical sympathetic chain and includes the stellate ganglion. We compared the sympatholytic and analgesic effect of paravertebral block performed at the T2 level (T2 PVB) with that of SGB in patients with complex regional pain syndrome (CRPS) of the upper extremity.

Objectives: The aim of this study was to compare the sympatholytic property of T2 PVB with that of the conventional SGB in patients with CRPS of the upper extremity.

Study Design: Prospective, randomized cross-over trial.

Setting: University hospital pain center in Korea.

Methods: Fifteen patients with upper extremity CRPS were randomly assigned to 1 of 2 intervention methods (SGB or T2 PVB). After effects of the first block receded, the patients were crossed over to the second procedure. A difference in temperature increase between the treated side and the opposite side (ΔT) $\geq 1.5°C$ was considered as a successful primary outcome. Rate of successful primary outcome, degree of pain reduction, duration of effect, and patient satisfaction scores were compared between the 2 intervention methods.

Results: Rate of successful primary outcome ($\Delta T \geq 1.5°C$) was significantly higher in the T2 PVB cases than in the SGB cases (80.0% vs. 20.0%; $P = 0.003$). Numeric Rating Scale scores after the procedure were significantly lower in the T2 PVB group. Patient satisfaction scores were significantly higher, and the duration of the block was significantly longer in the T2 PVB cases than in the SGB cases.

Limitations: The relatively small sample size from a single center, and the lack of standardization of the injected volume of T2 PVB and SGB were limitations.

Conclusions: T2 PVB showed superior sympatholytic effect than SGB; other clinical outcomes were also better with T2 PVB than with SGB. T2 PVB can be a useful option for producing sympatholytic and analgesic effect in patients with CRPS of the upper extremity.

Key words: Sympathetic block, Complex Regional Pain Syndrome, paravertebral block, stellate ganglion block

Stellate ganglion block (SGB) has been frequently used to treat intractable pain in the upper extremities, including complex regional pain syndrome (CRPS) (1). However, in clinical practice, the location of the needle tip during SGB is actually at the middle sympathetic ganglion located at the C6 or C7 level. Moreover, in many cases, SGB alone may not provide adequate sympatholysis in the upper extremities (2,3).

Kuntz fibers, which arise from the second and third thoracic sympathetic ganglion (TSG), directly connect to the brachial plexus bypassing the stellate ganglion (SG) or middle cervical ganglion, and are well described (4,5).

The positive effects of TSG block (TSGB) in CRPS have been reported (1,6). However, when TSGB is performed, the needle tip should be inserted lateral to the second vertebral body below the costovertebral articulation of the second rib; this requires technical expertise to avoid the complication of pneumothorax (7,8).

The paravertebral space contains the spinal root, communicating rami, and the sympathetic chain. Therefore, during a paravertebral block (PVB), the injectate could spread along the sympathetic chain (9). A potential pathway to the SG has been described in a previous cadaveric study (10). If a PVB is administered with a local anesthetic using sufficient volume at the second or third thoracic level, the injectate would be able to reach the SG as well as the TSG.

Although sympatholytic phenomena after PVB have been reported (11,12), the sympatholytic effect of PVB has never been evaluated as a treatment option for management of neuropathic pain, such as CRPS, to date.

The primary aim of this study was to compare the sympatholytic property of PVB performed at the T2 level (T2 PVB) with that of the conventional SGB in patients with CRPS of the upper extremity.

METHODS

The study was approved by the institutional ethics committee of the Daejeon St. Mary's Hospital, Daejeon, Republic of Korea. The trial was registered in the Clinical Trial Registry of Korea (trial registration number KCT0002270) before enrolment of the first participant. Written informed consent was obtained from each patient who participated in this study.

Patients

Fifteen patients with upper extremity CRPS were enrolled between March 2017 and January 2018. All the patients met the Budapest research criteria for CRPS recommended by the International Association for the Study of Pain (13). Patients with unilateral CRPS of the upper extremity, aged 19 years and over were included in the study. Patients aged < 19 years, patient refusal, infection, coagulopathies, pregnancy, and allergy to the drugs used were excluded from the study. Patients with severe psychiatric disorders that could influence the answers to the questionnaire, and patients with vascular disease that could affect the measurement of temperature changes were also excluded from the study.

Patients were randomly assigned to 1 of the 2 procedures (SGB or T2 PVB) using a random allocation program and received the first procedure. In cases of patients with chronic CRPS, according to our clinical experience, the effects of the procedures were usually no more than a few days; therefore, we set the washout period to 7 days. After the washout period, the patients were crossed over to the second procedure, and as a result all patients were given both SGB and T2 PVB during the study period (Fig. 1).

Procedure

T2 PVB

With the patient in the prone position, the site to be injected was disinfected with povidone-iodine. The skin was anesthetized using 1% lidocaine. A 22-G Tuohy needle was inserted under fluoroscopic guidance toward the transverse process of the second thoracic vertebra of the CRPS affected side. After contact with the bone, the direction of the needle was changed, and the needle was advanced under the transverse process. Paravertebral space was confirmed by using the loss of resistance technique, and 2 to 3 mL of contrast medium (Iobrix inj. 300, Accuzen, Seoul, Korea) was injected to check if the needle was properly inserted (Fig. 2 A-D).

Digital subtraction angiography was used to confirm the absence of intravascular contrast medium spread. After confirming that there was no sign of intravascular spread or pneumothorax, 10 mL of 1% lidocaine was injected as in previous studies (14,15).

SGB

The patients were placed in the supine position, and the head was turned 15 to 20 degrees to the opposite side of the site to be treated. The site to be injected was disinfected with povidone-iodine. A 5- to 12-MHz linear ultrasound transducer (X-Porte, SonoSite, Bothell, WA) was used to identify the transverse process of the sixth cervical vertebra. A color Doppler image was used to confirm the location of vessels. A 25-G needle was carefully inserted by positioning the needle tip superficial to the longus colli muscle and under the prevertebral fascia (Fig. 2 E,F). After confirming that there was no blood on aspiration, 5 mL of 1% lidocaine, a commonly recommended volume for ultrasound-guided SGB (16), was injected.
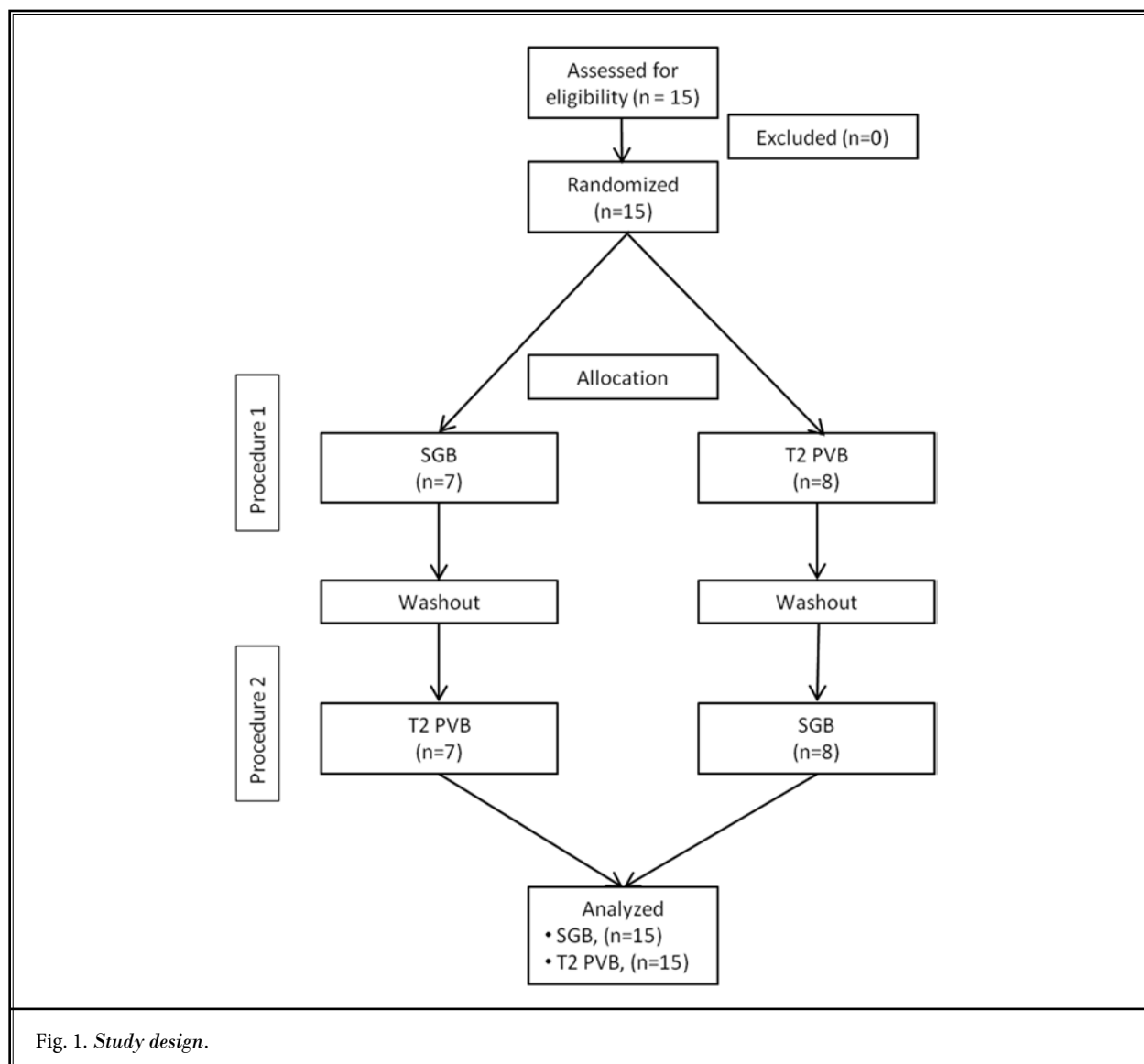
Fig. 1. *Study design*.

Measurement of Outcomes

Temperature was measured at the volar aspect of the index finger of both hands before the procedure, and at 5, 10, 15, and 20 minutes after the procedure using a touch thermometer (Patient monitor VM 8; Phillips Inc., Amsterdam, the Netherlands).

Primary Outcome

A difference in temperature increase between the treated side and the opposite side (ΔT) of 1.5°C or more was considered to yield a successful primary outcome. The ΔT was obtained with the following formula, 20 minutes after the procedure, as per the guidelines in previous studies (2,17): ΔT = temperature increase on the treated side – temperature increase on the opposite side.

Secondary Outcome

Numeric Rating Scale (NRS-11) was used for the evaluation of immediate effect on pain (before and 20 minutes after the procedure). We asked the patients about the time for NRS-11 scores to return to preprocedure levels. We also assessed patient satisfaction and improvement using the global perceived effect (GPE) scale on a 7-point Likert scale (Table 1) (18). Hemodynamic changes and other neurologic complications
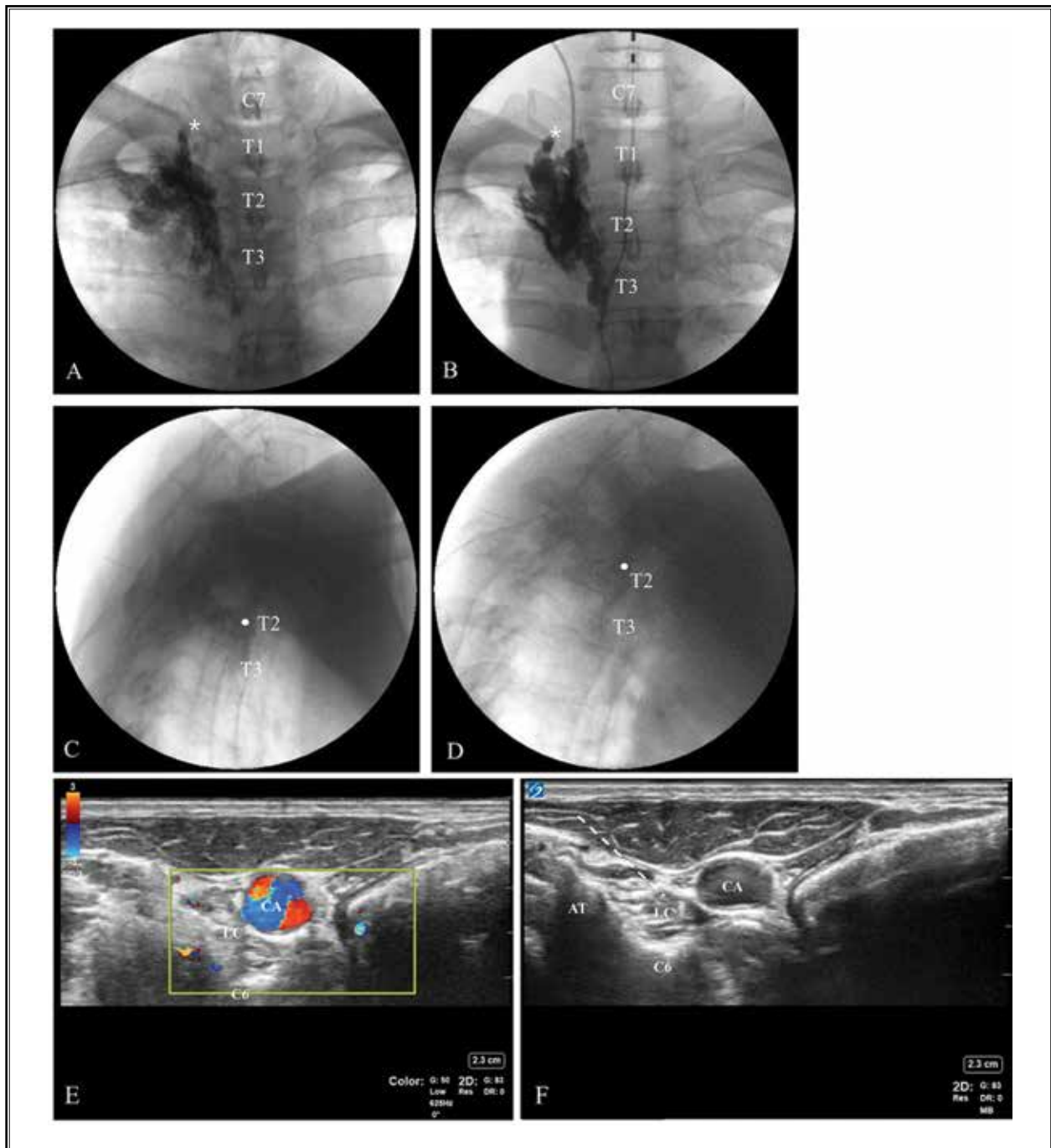
Fig. 2. *Images of fluoroscopy-guided T2 PVB and ultrasound-guided SGB. (A,B) Anteroposterior view of fluoroscopic image. (C,D) Lateral view of fluoroscopic image. Contrast media has spread to the location of the TSG (white circle) and near the anatomic location of the SG (asterisk). (E) Carotid artery was identified in color Doppler mode at the C6 level. (F) A needle was advanced under the prevertebral fascia on the surface of the longus colli muscle. AT: Anterior tubercle of the transverse process of C6; CA: Carotid artery; LC: Longus colli muscle; T: Thyroid; White dotted line: Trajectory of the needle.*

after the procedure were also evaluated. All measurements were recorded by doctors not associated with the study.

Statistical Analysis

According to our preliminary clinical experience, the rate of achieving $\Delta T \geq 1.5°C$ was 22% (2/9) in SGB and 75% (6/8) in T2 PVB. The sample size to establish clinical significance between the 2 block methods was calculated to be 13 patients with a significance level of 0.05 and power of 80%. Considering a possible withdrawal rate of 15%, a sample size of 15 patients was chosen.

Data are presented as mean ± standard deviation for continuous variables. Data normality were evaluated using the Kolmogorov–Smirnov test. Continuous variables were compared using independent t test. For categorical variables, the chi-square test or the Fisher exact test was used. Repeated measures analysis of variance was used to assess changes in temperature and hemodynamic parameters over time.

All data were analyzed using SPSS version 18.0 (SPSS Inc., Chicago, IL), and *P* values < 0.05 were considered statistically significant.

Results

A total of 15 patients participated in the study, and no patient dropped out during the study. The demographic characteristics of the patients are described in Table 2.

Sympatholytic Property

The ΔT values were significantly greater in T2 PVB than SGB (T2 PVB: 2.37 ± 1.21°C; SGB: 0.77 ± 0.51°C; *P* < 0.0001). Successful primary outcome ($\Delta T \geq 1.5°C$) was observed in 3 of 15 patients who underwent SGB (20.0%) and in 12 of 15 patients who received T2 PVB (80.0%). These differences were statistically significant (*P* = 0.003) (Table 3).

Eight of 15 patients (53.3%) who underwent SGB and 13 (86.7%) of 15 patients who underwent T2 PVB showed positive Horner's sign, but these differences were not statistically significant (*P* = 0.109).

Temperature Increase Over Time for each Method

Regarding temperature increase (difference between baseline temperature and temperature at a certain time point), there was no significant temperature increase over time on the contralateral side with both methods.

Table 1. *GPE: Likert scale 7-point scoring system.*

Score	% of Change
7	≥ 75% improvement
6	50%-74% improvement
5	25%-49% improvement
4	0%-24% improvement
3	0%-24% worsening
2	25%-49% worsening
1	50%-74% worsening
0	≥75% worsening

Table 2. *Patient characteristics, data of patients*

Gender, n (male/female)	Age (years)	Side of Block, n (right/left)	Duration of CRPS (months)
13/2	49.33 ± 9.28	9/6	58.00 ± 28.50

CRPS: complex regional pain syndrome.

Table 3. *Sympatholytic property.*

	SGB, n = 15	T2 PVB, n = 15	P value
ΔT	0.77 ± 0.51°C	2.37 ± 1.21°C	< 0.001#
Successful primary outcome ($\Delta T \geq 1.5°C$), n (%)	3/15 (20%)	12/15 (80%)	0.003*

ΔT: Difference in temperature increase between the treated side and the opposite side.
*P < 0.05.
#P < 0.001.

Although the temperature increased with time on the side at which the SGB was performed, the temperature increase over time between the SGB side and the contralateral side was not significantly different (*P* = 0.128). There was also no significant difference in temperature increase between both sides at each time point (Fig. 3A).

By contrast, the temperature increase over time was significantly higher on the side at which T2 PVB was performed than on the contralateral side (*P* < 0.0001). In addition, the temperature increases on the T2 PVB side were significantly greater than those on the contralateral side at all time points (Fig. 3B).

Clinical Outcomes

There was no significant difference in the baseline NRS-11 score before each procedure (SGB: 8.00 ± 0.38
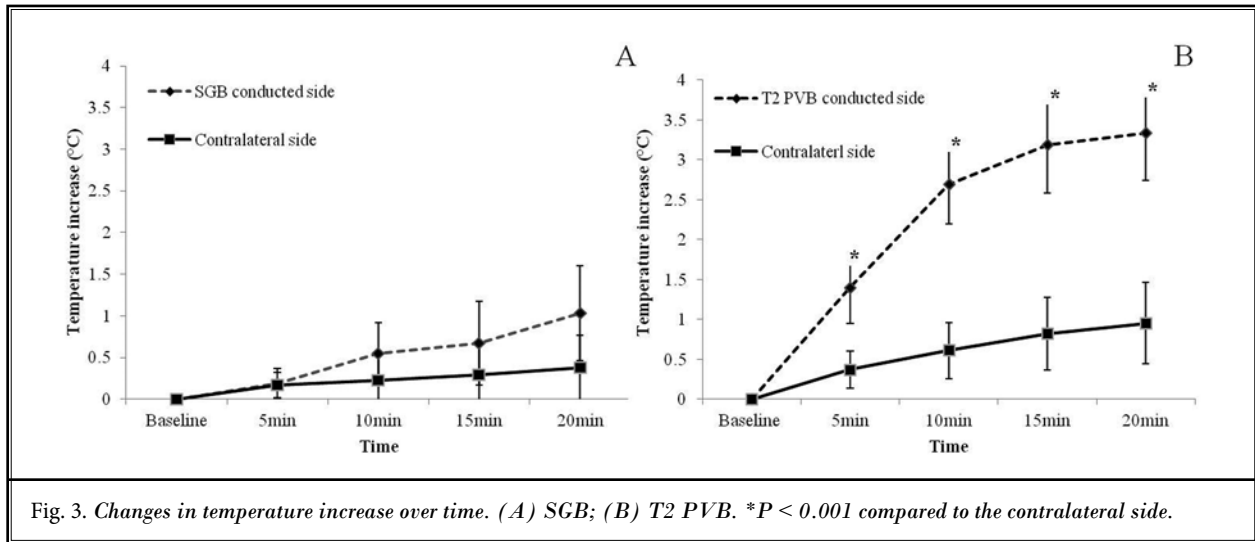
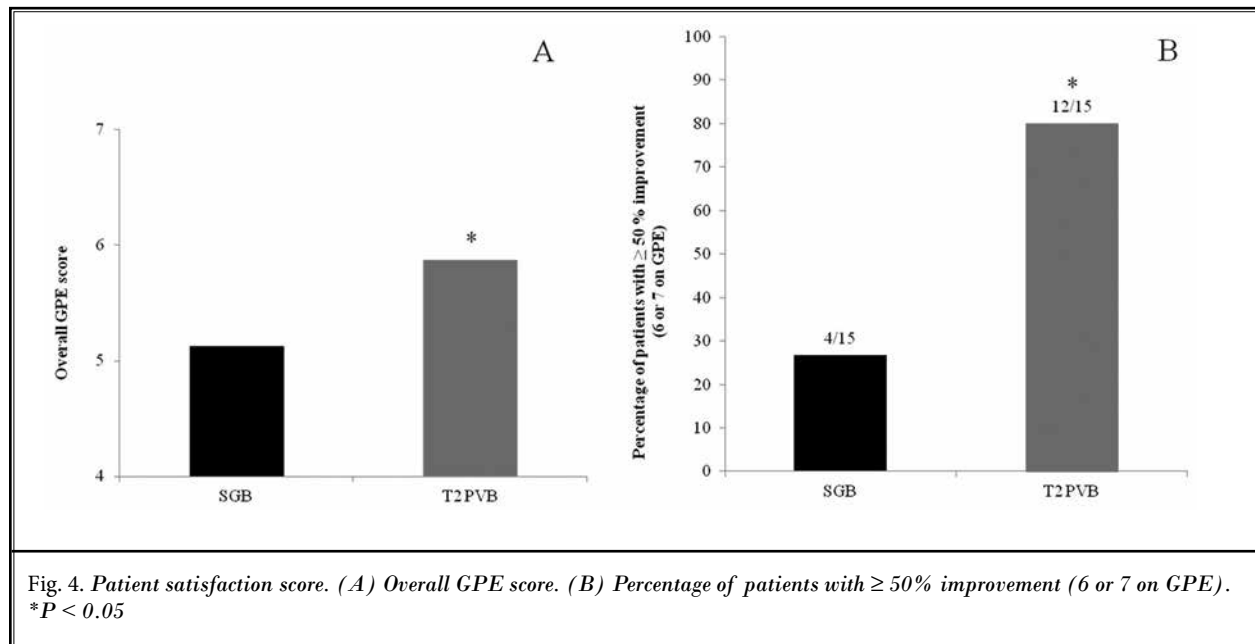Fig. 3. *Changes in temperature increase over time. (A) SGB; (B) T2 PVB. *P < 0.001 compared to the contralateral side.*

Fig. 4. *Patient satisfaction score. (A) Overall GPE score. (B) Percentage of patients with ≥ 50% improvement (6 or 7 on GPE). *P < 0.05*

vs. T2 PVB: 7.87 ± 0.51; *P* = 0.43); however, the NRS-11 score at 20 minutes after the procedure was significantly lower in the patients who underwent T2 PVB than in those who underwent SGB (SGB: 5.27 ± 1.22 vs. T2 PVB: 3.93 ± 1.27; *P* = 0.007).

The overall GPE score was significantly higher in the T2 PVB cases than in the SGB cases (SGB: 5.13 ± 0.64 vs. T2 PVB: 5.87 ± 0.91; *P* = 0.017) (Fig. 4A), and the percentage of patients reporting > 50% improvement (6 or more on GPE score) was significantly higher in the T2 PVB cases than in the SGB cases (SGB: 26.7%, 4/15 vs.

T2 PVB: 80.0%, 12/15; *P* = 0.003) (Fig. 4B).

The duration of effect (time taken for NRS-11 score to return to preprocedure levels) was significantly longer in the patients who underwent T2 PVB than in those who underwent SGB (SGB: 9.26 ± 2.21 hours vs. T2 PVB: 37.20 ± 12.14 hours; *P* = 0.015).

Hemodynamic Changes after the Procedure, Contrast Medium Spreading Pattern, and Presence of Complications

With both methods, hypotension (systolic pressure

< 90 mmHg) was not observed during the periprocedural period. There was no intravascular injection during T2 PVB. Epidural spreading of the contrast medium during T2 PVB was observed in 3 out of 15 patients.

There were no specific neurologic symptoms including motor or sensory deficits. Other complications such as dyspnea or dizziness were not observed.

DISCUSSION

In this study, superior clinical outcomes including greater sympatholytic property, greater pain reduction immediately after the procedure, longer duration of effect, and higher subjective patient satisfaction scores were achieved with T2 PVB compared to SGB.

It is known that the function of the sympathetic nervous system is reduced in chronic neuropathic conditions such as CRPS (19,20). In such a circumstance where the sympathetic outflow is already reduced, the clinical signs induced by the sympathetic block may be less significant than the clinical signs induced by the sympathetic block in the absence of sympathetic outflow disturbance. SGB alone would not be able to obtain satisfactory sympatholytic effect on the upper extremities in such a situation. In a previous SGB study, the success rate of $\Delta T \geq 1.5°C$ was reported to be just 27% (2).

Although it is controversial as to whether the sympathetic block is effective in CRPS (21), it is commonly performed in clinical practice and is one of the important options for management of upper extremity neuropathic pain (1). Therefore, it would be meaningful to develop a more effective and safe method of sympathetic blockade.

It has already been demonstrated through magnetic resonance imaging and cadaveric studies that the injectate can flow forward to the sympathetic chain during PVB (9,10). Horner's sign after high-thoracic PVB has also been reported (11,12). In the present study, we observed that the contrast medium had spread to the location of the TSG on the fluoroscopic image, and we confirmed that the contrast medium spreads close to the actual SG location on the anteroposterior view of the fluoroscopic image (Fig. 2). Based on these results, the greater sympatholytic property in T2 PVB compared with SGB seems to be owing to the simultaneous blocking of TSG and SG during T2 PVB. Therefore, we believe that T2 PVB can achieve more profound sympatholysis of the upper extremities than SGB alone.

The lack of standardization of the injected volume of T2 PVB and SGB is a limitation of this study. The volume of 2 to 5 mL of local anesthetics was generally recommended to ensure sympatholytic effects during SGB (16). In our pain clinic, we also used 5 mL of injectate for SGB.

In previous PVB studies (14,15), volumes of 10 mL of local anesthetics were used. According to our clinical experience with T2 PVB, a volume of 10 mL of injectate was also appropriate for covering the SG and the TSG.

We thought that comparative study using the volumes commonly used would yield clinically more practical results. Therefore, in this study we used 5 mL and 10 mL of local anesthetics for SGB and T2 PVB, respectively.

The accurate extent of spread of the injectate after T2 PVB was not evaluated by further imaging techniques, such as 3-dimensional computed tomography, although we confirmed that the contrast medium spread to the location of the TSG and spread close to the actual SG location on the fluoroscopic image. This may also be a limitation of this study.

A relatively small sample size collected from a single hospital might be another limitation of this study

CONCLUSIONS

T2 PVB showed superior sympatholytic effect than SGB, and clinical results, such as degree of pain reduction, duration of effect, and patient satisfaction were also superior to SGB. To our knowledge, the present study is the first to evaluate the sympatholytic property of high thoracic PVB as a treatment option in a chronic intractable pain condition, such as CRPS. Future studies in various neuropathic conditions in the upper extremities would be needed to determine if T2 PVB can be used safely and effectively as a treatment option.

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