Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

CLINICAL TRIAL REPORT

Determination of the ED90 and ED99 of Liposomal versus Conventional Bupivacaine for Ultrasound-Guided Stellate Ganglion Block: A Biased-Coin Design Study

Litong Yang[1,*], Junxiang Liu[2,*], Yutong Yang[3], Haodong Zhao[4], Zhidong Fan[3], Guangfen Yin[3], Qinghang Xuan[3]

[1]Department of Anesthesiology, Xiangyun County People's Hospital, Dali, Yunnan, People's Republic of China; [2]Department of Orthopedics, Xiangyun County People's Hospital, Dali, Yunnan, People's Republic of China; [3]Department of Anesthesiology, The First Affiliated Hospital of Dali University, Dali, Yunnan, Peoples Republic of China; [4]Department of Trauma Orthopedics, the First Affiliated Hospital of Dali University, Dali, Yunnan, People's Republic of China

*These authors contributed equally to this work

Correspondence: Qinghang Xuan, Department of Anesthesiology, The First Affiliated Hospital of Dali University, Dali, Yunnan, People's Republic of China, Tel +8615253066603, Email xuanqinghang@163.com

Background: Local anesthetics commonly used for ultrasound-guided stellate ganglion block (SGB) have a relatively short duration of action (6–12 hours). Liposomal bupivacaine, utilizing a multivesicular liposome sustained-release technology, can extend the block duration to over 72 hours, offering a potential option for prolonged sympathetic blockade. Determining its optimal effective dose relative to conventional bupivacaine is crucial for balancing prolonged efficacy with safety.

Methods: All patients received ultrasound-guided SGB, successful blockade was explicitly defined as the onset of Horner syndrome (ptosis, miosis, anhidrosis) within 30 minutes post-injection. For the 0.5% bupivacaine hydrochloride group, the initial volume was 1.6 mL. The volume was adjusted using a biased-coin up-and-down sequential design with a step size of 0.2 mL. The study endpoint was 45 successful blocks, and the ED90 was calculated using isotonic regression. The liposomal bupivacaine group followed an identical design with an initial volume of 1.6 mL (266 mg/20 mL) and a step size of 0.4 mL.

Results: The ED90 for 0.5% bupivacaine hydrochloride was 2.07 mL (95% CI: 1.99, 2.57), and the ED99 was 2.37 mL (95% CI: 2.33, 3.05 mL). The ED90 for liposomal bupivacaine was 3.75 mL (95% CI: 2.90, 5.17 mL), and the ED99 was 4.35 mL (95% CI: 4.22, 5.36 mL).

Conclusion: Volumes of approximately 2.1 mL of bupivacaine hydrochloride and 3.8 mL of liposomal bupivacaine can be expected to achieve near-complete stellate ganglion blockade. While liposomal bupivacaine holds promise for long-duration therapy, dosing must be cautious due to the prolonged course of potential complications.

Keywords: local anesthetics, dose-response relationship, liposomal bupivacaine, bupivacaine hydrochloride, stellate ganglion block, ultrasound-guided

Introduction

Stellate ganglion block (SGB) is a classic and widely used sympathetic nerve blockade technique, playing a significant role in pain management, neuromodulation, and the treatment of autonomic nervous system disorders. Its indications encompass complex regional pain syndrome (CRPS), insomnia and other psychological conditions, immune dysfunction-related diseases, and it shows potential value in treating certain arrhythmias.[1–3] The stellate (cervicothoracic) ganglion is anatomically located at the C7 and T1 vertebral levels. The clinical intervention commonly termed "SGB" is technically a regional block performed at the C6 transverse process. Under ultrasound guidance, the local anesthetic is injected into

https://doi.org/10.2147/DDDT.S609398
Received: 15 March 2026
Accepted: 14 May 2026
Published: 19 May 2026

the fascial plane between the longus colli muscle and the prevertebral fascia, with the intent of caudal spread to the vicinity of the stellate ganglion.

Throughout this manuscript, "SGB" denotes this ultrasound-guided C6 approach for cervicothoracic sympathetic blockade. In traditional practice, SGB often uses short-acting local anesthetics, which typically provide blockade for no more than 12 hours. This necessitates repeated procedures, increasing patient burden and risks such as hematoma, infection, and nerve injury. Therefore, a technique that significantly prolongs the duration of sympathetic blockade after a single injection is urgently needed. Liposomal bupivacaine is a novel, extended-release formulation of bupivacaine. It utilizes a multivesicular liposome delivery system to encapsulate the drug, allowing for sustained release at the injection site and providing analgesic effects that can last over 72 hours. Some studies report extended analgesia with liposomal bupivacaine in peripheral nerve blocks, its overall efficacy compared to conventional agents remains a topic of discussion, with other trials showing equivocal benefits.[4–7] Regardless, its optimal dose, safety, and comparison with traditional anesthetics for SGB lack evidence-based research.

While it has shown good efficacy and safety in peripheral nerve blocks,[4,5] its optimal dose, safety, and comparison with traditional anesthetics for SGB lack evidence-based research. Although the ED90 of 1% lidocaine for SGB has been reported to be approximately 3.83 mL, the exact effective doses (ED90/ED99) of both liposomal bupivacaine and bupivacaine hydrochloride for this procedure remain undetermined.[8] Furthermore, a direct pharmacodynamic comparison between these two bupivacaine formulations in the context of SGB is currently lacking.

Therefore, we hypothesized that the ED90 and ED99 of liposomal bupivacaine for ultrasound-guided SGB would be different from those of conventional bupivacaine hydrochloride. This study employed a biased-coin up-and-down sequential design (BCD-UDM) to determine the 90% and 99% effective doses (ED90 and ED99) for both bupivacaine hydrochloride and liposomal bupivacaine in SGB. This method offers greater precision in dose-finding compared to traditional fixed-dose or Massey up-and-down methods,[9] providing a scientific basis for optimizing the use of liposomal bupivacaine in SGB.

Materials and Methods

This study was approved by the Ethics Committee of the First Affiliated Hospital of Dali University (Approval No.: SFY20251231001), on 31 December 2025. The trial was registered on January 6, 2026, at the Chinese Clinical Trial Registry (ChiCTR), which is a primary registry of the WHO International Clinical Trials Registry Platform (Registration ID: ChiCTR2600116174). All participants provided written informed consent in accordance with the Declaration of Helsinki.

Inclusion Criteria:Age between 18 and 75 years, regardless of gender, ASA physical status classification I–III, BMI between 18.0 and 28.0 kg/m^2.

Exclusion Criteria:Known allergy to local anesthetics,Contraindications to nerve block (eg, coagulation disorders, sepsis, tumor or infection at the puncture site, or other relevant conditions), Cervical spine deformity, Significant cervical trauma or surgical scarring, Psychiatric or central nervous system disorders, or inability to cooperate, Severe cardiac, pulmonary, or other major organ dysfunction,Pregnancy or lactation.

Blinding

Due to the distinct volume regimens between the liposomal bupivacaine and bupivacaine hydrochloride groups mandated by the biased-coin design, it was not feasible to blind the physician performing the procedure (the operator). However, a single-blind approach was implemented for the patients. Furthermore, to minimize assessment bias, the researcher responsible for evaluating the primary outcome (the presence of Horner's syndrome within 30 minutes post-injection) was blinded to the specific drug and volume administered to each patient.

Ultrasound-Guided Stellate Ganglion Block Procedure

The patient was placed in the supine position with the neck slightly extended and the head turned to the contralateral side to adequately expose the cervical region on the puncture side. A high-frequency linear ultrasound probe (Ultrasound device: KONICA SONIMAGE HS1, Shanghai, China; Ultrasound probe: 18 MHz), sterile probe cover, coupling gel, and

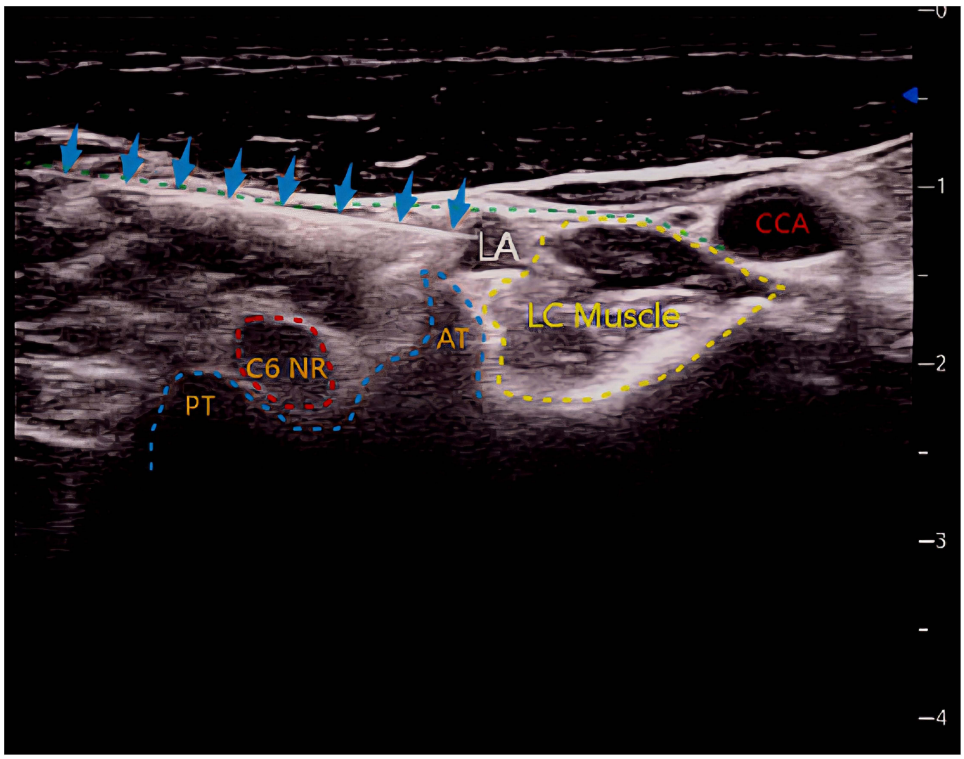

Figure 1 Ultrasound-Guided Stellate Ganglion Block Procedure: Anatomical Landmarks and Needle Placement (Green dashed line: Prevertebral fascia, Blue arrow points to the needle).
Abbreviations: LA, Local anesthetic; CCA, Common carotid artery; LC Muscle, Longus Colli Muscle; C6 NR, The 6th cervical nerve root; AT, Anterior tubercle of the transverse process of C6; PT, Posterior tubercle of the transverse process of C6.

local disinfection supplies were prepared. A 22-gauge, 10-cm needle (Sterile injection needle: 0.7×80 mm, Zhejiang Kangdelai Medical Device Co., Ltd., Zhejiang, China) was selected, and the local anesthetic solution was prepared.

Under ultrasound guidance, key anatomical structures were identified from superficial to deep: thyroid gland, common carotid artery, longus colli muscle, and the C6 transverse process. The target for injection was the fascial plane between the of the longus colli muscle and the of the prevertebral fascia. The ganglion is below the prevertebral fascia and above longus colli. The stellate ganglion itself is not directly visualized on ultrasound; it is located more caudally, anterior to the C7/T1 vertebrae. The objective of the C6 approach is to deposit local anesthetic within this fascial plane, allowing for caudal spread to reach the ganglion region.

Using an in-plane technique, the needle was inserted from the lateral edge of the ultrasound probe, ensuring the entire needle shaft (including the tip) remained visible on the ultrasound screen throughout the procedure. Under real-time ultrasound guidance, the needle was advanced toward the fascial plane between the anterolateral aspect of the C6 vertebral body and the longus colli muscle, carefully avoiding the common carotid artery, thyroid gland, and vertebral artery. Once the needle tip reached the target fascial plane, aspiration was performed to confirm the absence of blood, air, or cerebrospinal fluid. A small test dose of local anesthetic was injected slowly under ultrasound visualization to observe its spread. The ideal distribution pattern appeared as a crescent-shaped or teardrop-shaped hypoechoic area superficial to the longus colli muscle, with slight anterior-lateral displacement of the carotid artery (Figure 1). After confirming correct needle placement, the remaining local anesthetic was injected, and satisfactory spread within the target space was monitored in real time.Upon completion of the injection, the needle was promptly withdrawn, and the puncture site was covered with a sterile dressing. The patient remained in the supine position for rest, with close monitoring of vital signs.

https://doi.org/10.2147/DDDT.S609398

Determination of ED90 for Bupivacaine Hydrochloride in SGB

This study employed a biased-coin up-and-down sequential design (BCD-UDM). The initial dose for the first patient was set at 1.6 mL of 0.5% bupivacaine hydrochloride. The injection volume was adjusted based on the previous patient's block outcome, with a step size of 0.2 mL between adjacent concentrations. If SGB failed in a patient, the subsequent patient received an increased volume of 0.2 mL. Conversely, if SGB was successful in the previous patient, the volume for the next patient was determined by biased-coin randomization: an 11% probability of decreasing the volume by 0.2 mL and an 89% probability of maintaining the same volume. This part of the study was terminated after achieving 45 successful blocks (Figure 2). The ED90 and ED99 values with their 95% confidence intervals were calculated using isotonic regression analysis.

Determination of ED90 for Liposomal Bupivacaine in SGB

An identical BCD-UDM methodology was applied for data collection. The first patient received 1.6 mL of liposomal bupivacaine, with subsequent volumes determined by the preceding patient's block outcome using a dose increment of 0.4 mL. If SGB failed in a patient, the next patient received an increased volume of 0.4 mL. For successful blocks, the subsequent volume was determined by biased-coin randomization: an 11% probability of decreasing by 0.4 mL and an 89% probability of maintaining the current volume. The study continued until 45 successful blocks were achieved (Figure 3). The ED90 and ED99 values with 95% confidence intervals were calculated through isotonic regression analysis.

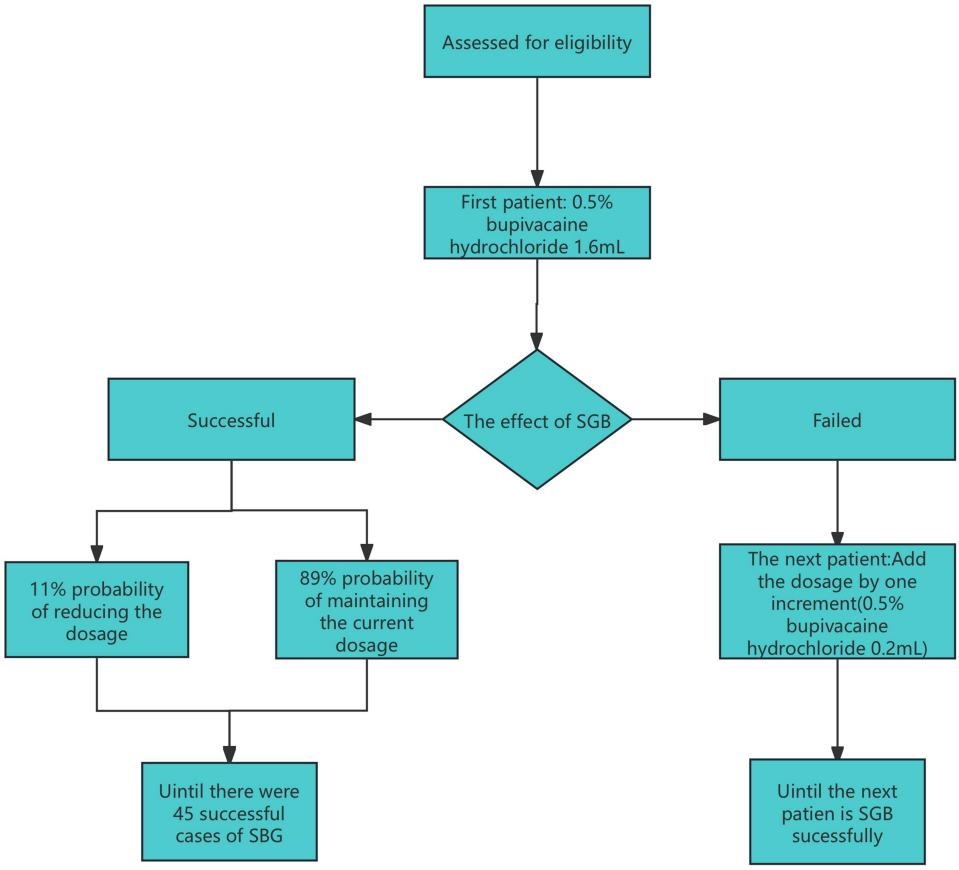

Figure 2 Consort diagram of Bupivacaine Hydrochloride in SGB.

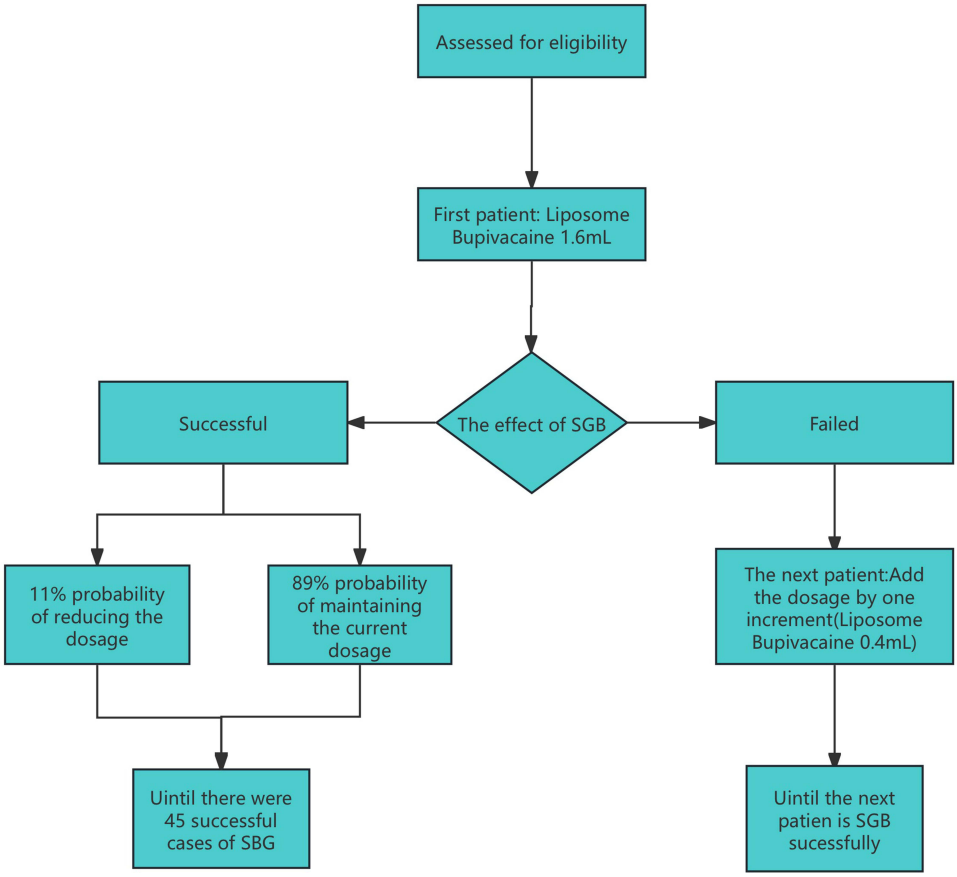

Figure 3 Consort diagram of liposomal bupivacaine in SGB.

Outcome Measures

Primary Outcome

SGB block efficacy: Successful blockade was defined by the presence of any of the following characteristics within 30 minutes post-procedure:Horner syndrome (ptosis, miosis, anhidrosis).[10] Horner syndrome was assessed independently by two anesthesiologists; the block was deemed successful only when both observers confirmed its presence.

Secondary Outcomes

Documentation and duration of follow-up for adverse events, including: hoarseness, dysphagia, weakness in the blocked upper extremity, local hematoma formation, pneumothorax, and local anesthetic systemic toxicity (LAST). Adverse events were monitored and documented from the time of intervention until 72 hours post-procedure (or until complete resolution of any persistent adverse event, whichever was longer).

Statistical Analysis

Statistical analyses were performed using R version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria), with graphical representations created using GraphPad Prism 9.0 (GraphPad Software, CA, USA). Normally distributed continuous variables were expressed as mean ± standard deviation ($\overline{X} \pm S$), while categorical data were presented as counts (percentages). Intergroup comparisons utilized *t*-tests for normally distributed data and chi-square tests for non-normally distributed data.The biased-coin up-and-down sequential method was employed to calculate the ED90 and ED99 for ultrasound-guided SGB using both 0.5% bupivacaine hydrochloride and liposomal bupivacaine. The following parameters were applied:$\Gamma = 0.1$ (indicating a 10% probability of block failure), $b = \Gamma/(1-\Gamma) = 0.11$ (resulting in an 11% probability of dose reduction and 89% probability of maintaining the current dose level for subsequent patients following

https://doi.org/10.2147/DDDT.S609398

a successful block).[10] ED90 and ED99 values with 95% confidence intervals were determined using centered isotonic regression analysis.

Sample Size Calculation

The isotonic regression analysis required the number of successful blocks to be a multiple of 9 and exceed 40 cases. Therefore, the estimated sample size was set at 54 patients per study group to ensure adequate statistical power for the dose-response analysis.

Results

A total of 110 patients were enrolled in this study. Among them, 56 patients participated in Part 1 (ED90 of 0.5% bupivacaine hydrochloride). Successful blockade was achieved in 45 patients, while 11 patients experienced block failure. The ED90 of 0.5% bupivacaine hydrochloride was 2.07 mL (95% CI: 1.99–2.57), and the ED99 was 2.37 mL (95% CI: 2.33–3.05 mL), as shown in Figure 4.

54 patients participated in Part 2 (ED90 of liposomal bupivacaine). Successful blockade was achieved in 45 patients, with 9 failures. The ED90 of 0.5% liposomal bupivacaine was 3.75 mL (95% CI: 2.90–5.17 mL), and the ED99 was 4.35 mL (95% CI: 4.22–5.36 mL), as shown in Figure 5.

ED90 Study of Bupivacaine Hydrochloride

In the first part of the study on the ED90 of bupivacaine hydrochloride, involving 56 patients, the age was 44.5±13.5 years, with females comprising 57%. The baseline characteristics of this study group are presented in Table 1.

ED90 Study of 0.5% Liposomal Bupivacaine

In the second part of the study on the ED90 of 0.5% liposomal bupivacaine, involving 54 patients, the mean age was 44 ±12.6 years, with females comprising 59%. The baseline characteristics of this study group are presented in Table 2.

In the ED 90 study of ultrasound-guided SGB using 0.5% bupivacaine hydrochloride, five volume gradients were used: 1.6 mL, 1.8 mL, 2.0 mL, 2.2 mL, and 2.4 mL The block success rates for these different volumes were 33.3% (2/6), 63.6% (7/11), 95% (19/20), 80.0% (8/10), and 100% (9/9), respectively. Among the 56 patients included, hoarseness occurred in 2 patients (3.6%), with symptoms resolving within 6 hours after administration. The doses associated with hoarseness in these patients were 1.8 mL and 2.0 mL, respectively.

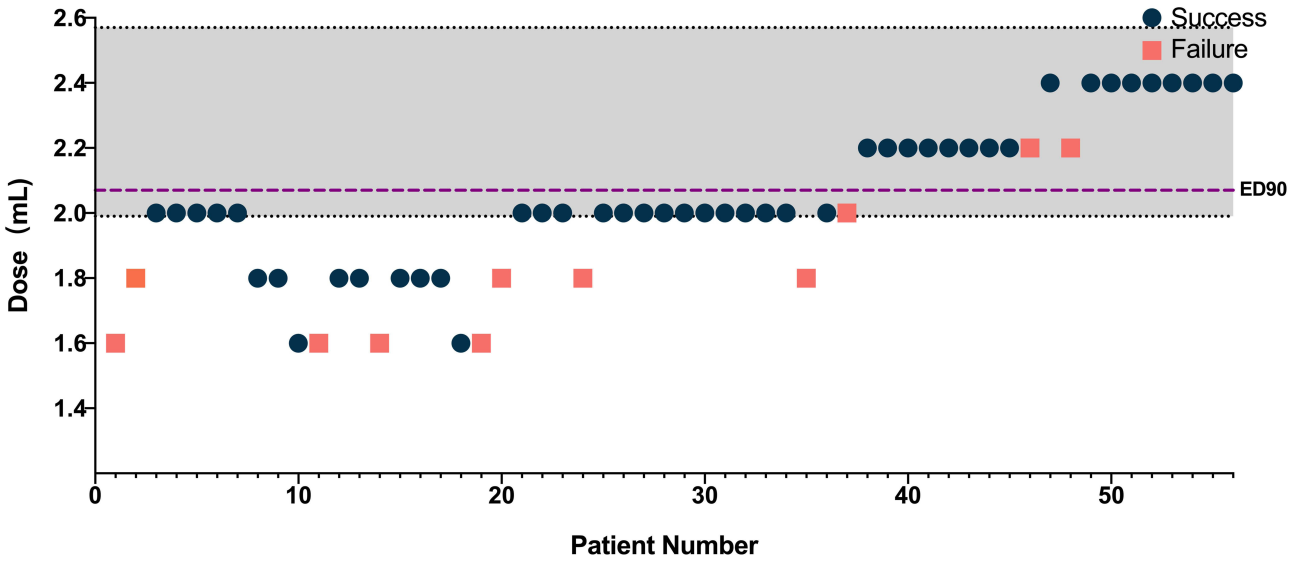

Figure 4 Patient sequential diagram for the Bupivacaine hydrochloride group (Purple dashed line indicates the ED90 dose; gray area between the black dashed lines represents the 95% confidence interval of ED90).

https://doi.org/10.2147/DDDT.S609398

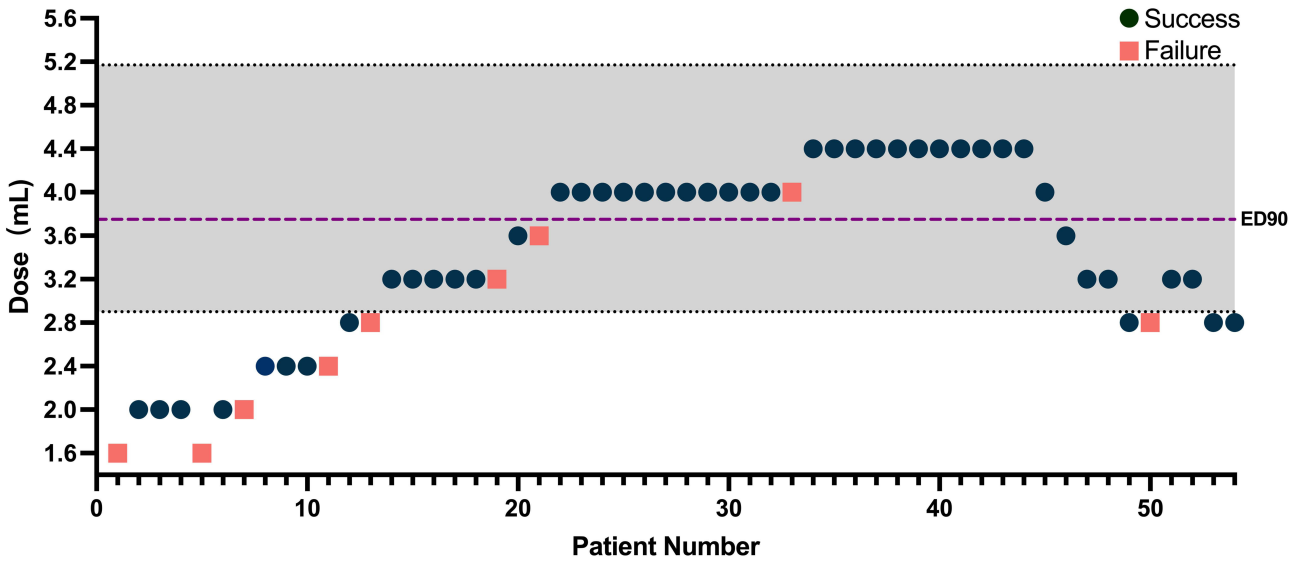

Figure 5 Patient sequential diagram for the Liposome Bupivacaine group (Purple dashed line indicates the ED90 dose; gray area between the black dashed lines represents the 95% confidence interval of ED 90).

In the ED 90 study of ultrasound-guided SGB using liposomal bupivacaine, eight volume gradients were used: 1.6 mL, 2.0 mL, 2.4 mL, 2.8 mL 3.2 mL, 3.6 mL, 4.0 mL, and 4.4 mL. The block success rates for these different volumes were 0% (0/2), 80% (4/5), 75% (3/4), 66.7% (4/6), 90% (9/10), 66.7% (2/3), 92.3% (12/13), and 100% (11/11), respectively. Among the 54 patients included, hoarseness occurred in 2 patients (3.7%), with symptoms resolving after

Table 1 Demographics of Patients Receiving Bupivacaine Hydrochloride for SGB

	n=56
Age (years)	44.5±13.5
Gender (Male/Female)	24/32
BMI (kg/m^2)	23.0±3.3
ASA (I/II/III)	
I	10
II	42
III	2

Table 2 Demographics of Patients Receiving Liposomal Bupivacaine for SGB

	n=54
Age (years)	44±12.6
Gender (Male/Female)	22/32
BMI (kg/m^2)	24.1±2.9
ASA (I/II/III)	
I	13
II	37
III	4

https://doi.org/10.2147/DDDT.S609398

60 hours and 72 hours, respectively. The doses associated with hoarseness in these patients were 3.2 mL and 4.0 mL, respectively.

Discussion

Stellate ganglion block (SGB) plays a significant role in the treatment of chronic sympathetic nerve-mediated conditions such as Complex Regional Pain Syndrome (CRPS) and hyperhidrosis. It has also demonstrated considerable efficacy in alleviating postoperative pain, improving insomnia, and managing refractory arrhythmias.[11–15] This study simultaneously determined the ED90 and ED99 of both bupivacaine hydrochloride and liposomal bupivacaine for SGB using the biased coin up-and-down sequential design. This method offers greater precision in exploring the minimum effective volume compared to traditional approaches, which is crucial for enhancing drug safety and reducing the risk of complications.[16] The dose escalation gradient was set at 0.2 mL for bupivacaine hydrochloride and 0.4 mL for liposomal bupivacaine, a design based on pre-trial results indicating that these dose differences produced distinguishable variations in block efficacy.

The most common complication of SGB is hoarseness, primarily caused by the spread of the local anesthetic to the recurrent laryngeal nerve.[17] Previous research indicated that the ED99 for 1% lidocaine is approximately 3.97 mL, whereas the typical clinical doses for short-acting local anesthetics often range from 5–10 mL. Such a volume, being multiples higher, significantly increases the risk of drug spread to the recurrent laryngeal nerve or brachial plexus.[8] Although bupivacaine hydrochloride carries a certain risk of cardiotoxicity and the SGB injection site is close to the internal carotid artery, lidocaine is often preferred in clinical practice. However, lidocaine has lower anesthetic potency, requiring a larger volume to achieve the same blocking effect.

The results of this study show that the ED90 and ED99 for 0.5% bupivacaine hydrochloride in SGB are 2.07 mL (95% CI: 1.98–2.56 mL) and 2.37 mL (95% CI: 2.33–3.05 mL), respectively. This represents a reduction of approximately 40% in the effective volume compared to the ED99 of 1% lidocaine (3.79 mL vs. 2.37 mL), suggesting that bupivacaine hydrochloride, while maintaining effective blockade, may reduce volume-related complications through lower-volumeadministration. Considering the relatively high cardiotoxicity of bupivacaine hydrochloride,[18] the ED 99 value of 2.37 mL (equivalent to 11.85 mg of 0.5% bupivacaine hydrochloride) is significantly below the threshold for cardiovascular toxicity, thus indicating a reduced risk of cardiovascular toxicity and, potentially, volume-related complications when used at this determined dose. The confidence intervals for the effective doses, especially for liposomal bupivacaine, are relatively wide. This reflects the inherent variability in individual response to nerve blocks, which can be influenced by anatomical differences, tissue characteristics, and the complex release kinetics of the liposomal formulation. While the isotonic regression method provides robust point estimates (ED90, ED99), the width of the CIs indicates the precision of these estimates in the studied population. Therefore, the ED values presented here should be interpreted as population estimates. In clinical practice, they serve as a scientifically informed starting point, and the optimal dose for an individual patient may lie within this range, necessitating careful observation and titration.

The primary advantage of liposomal bupivacaine, as an extended-release local anesthetic, in SGB is its ability to prolong the duration of sympathetic blockade, potentially replacing the need for repeated blocks and extending the therapeutic window.[19,20] However, as pain management patients are often treated in day wards, managing complications occurring outside the hospital becomes more challenging. Therefore, it is essential to precisely control the dosage at the minimum effective level. This study found that the ED90 and ED99 for liposomal bupivacaine are 3.75 mL (95% CI: 2.90–5.17 mL) and 4.35 mL (95% CI: 4.22–5.36 mL), respectively. Although the ED99 volume of liposomal bupivacaine is approximately 44% higher than that of bupivacaine hydrochloride, its sustained-release mechanism is designed to provide prolonged analgesia. This potentialfor longer duration, coupled with the effective dose established in this study, suggests it could besuitable for long-term pain management regimens. However, this application prospect requires confirmation in trials specifically designed to measure comparative block duration and long-term outcomes. Previous studies have indicated that due to the sustained-release characteristics of liposomal bupivacaine, its standalone application in peripheral mixed nerve blocks is associated with a relatively low success rate. However, this property may be beneficial in reducing recurrent laryngeal nerve block during stellate ganglion block (SGB). This is because the stellate ganglion, as a sympathetic ganglion, contains finer and unmyelinated nerve fibers, making it more susceptible to

blockade by liposomal bupivacaine. In contrast, the recurrent laryngeal nerve, being a mixed nerve, exhibits relatively lower sensitivity to sustained-release agents. Consequently, it is theorizedthat while achieving effective sympathetic blockade, the relative sensitivity of different nerve fibers might differentially influence the risk profile. However, this theoretical differential effect on nerve types, and its translation to a clinically meaningful reduction in complication risk, require direct investigation in future comparative studies.

In the safety assessment, hoarseness occurred in 2 out of 54 patients (3.7%) in the liposomal bupivacaine group (at doses of 3.75 mL and 4.0 mL), with symptoms resolving after 60 and 72 hours, respectively. In the bupivacaine hydrochloride group, hoarseness also occurred in 2 out of 56 patients (3.6%), with symptoms resolving within approximately 6 hours. The doses causing recurrent laryngeal nerve block in both groups were lower than their respective ED99 values, indicating that this complication cannot be entirely avoided even when using the minimum effective volume. Consequently, extra caution should be exercised in dose selection for liposomal bupivacaine due to its long duration of action.

In addition to extended-release local anesthetics, pulsed radiofrequency represents an alternative interventional therapy aimed at achieving prolonged neuromodulation of the stellate ganglion region. Current evidence suggests that the duration of therapeutic effect from pulsed radiofrequency may exceed that of conventional bupivacaine hydrochloride blocks.[21] However, direct comparative data on the efficacy and durability between pulsed radiofrequency and liposomal bupivacaine are still lacking. Against this backdrop, by determining the effective dose of liposomal bupivacaine, this study provides critical dosimetric evidence for this emerging long-acting pharmacological strategy.

Limitations

This study did not dilute the liposomal bupivacaine formulation. The reason is that dilution increases the injection volume, which could lead to wider drug spread and potentially increase the risk of blocking the recurrent laryngeal nerve or even more distant nerves. For unilateral recurrent laryngeal nerve blocks lasting over 72 hours, while the impact on respiratory safety is limited, it significantly reduces patient comfort and quality of life. Furthermore, as this was a dose-finding study, it cannot directly compare the analgesic duration or complication rates between the two local anesthetics for SGB. Related randomized controlled trials are currently underway. Furthermore, this study did not analyze the potential influence of individual anatomical characteristics (eg, sex, height, neck length) on the effective volume required for a successful SGB. Future research correlating such morphometric parameters with the minimum effective volume could facilitate more personalized dosing regimens.

Conclusion

The ED90 of bupivacaine hydrochloride and liposomal bupivacaine for ultrasound guided SGB to be 2.07 mL and 3.75 mL, respectively. Based on these ED90 values, an initial volume of approximately 2.1 mL or 3.8 mL is recommended for each drug to achieve effective blockade. The extended-release property of liposomal bupivacaine suggests a potential for prolonged effect, which must be balanced against the risk of similarly prolonged complications, as observed. Therefore, its use requires cautious, individualized dosing. These findings provide the first dose-response data and a foundation for the evidence-based application of liposomal bupivacaine in SGB.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of The First Affiliated Hospital of Dali University (Approval No.: SFY20251231001) on December 31, 2025. The trial was registered at the Chinese Clinical Trial Registry (ChiCTR), a primary registry of the WHO International Clinical Trials Registry Platform, on January 6, 2026 (Registration ID: ChiCTR2600116174).

Author Contributions

All authors made substantial contributions to the conception, study design, execution, acquisition of data, analysis and interpretation; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

The authors confirm that there is no funding to report for this study.

Disclosure

The authors declare that they have no competing interests.

References

1. Malik V, Shivkumar K. Stellate ganglion blockade for the management of ventricular arrhythmia storm. *Eur Heart J*. 2024;45(10):834–836. doi:10.1093/eurheartj/ehae083
2. Rae Olmsted KL, Bartoszek M, Mulvaney S, et al. Effect of Stellate Ganglion block treatment on posttraumatic stress disorder symptoms: a randomized clinical trial. *JAMA Psychiatry*. 2020;77(2):130–138. doi:10.1001/jamapsychiatry.2019.3474
3. Lipov EG, Joshi JR, Sanders S, et al. Effects of stellate-ganglion block on hot flushes and night awakenings in survivors of breast cancer: a pilot study. *Lancet Oncol*. 2008;9(6):523–532. doi:10.1016/S1470-2045(08)70131-1
4. Ilfeld BM, Eisenach JC, Gabriel RA. Clinical effectiveness of liposomal bupivacaine administered by infiltration or peripheral nerve block to treat postoperative pain. *Anesthesiology*. 2021;134(2):283–344. doi:10.1097/ALN.0000000000003630
5. Patel TD, Dusza M, Lee CT. Efficacy and safety of liposomal bupivacaine administration in the pediatric population: a scoping review of the literature.Anesthesiol. *Perioper Sci*. 2025;3(13). doi:10.1007/s44254-025-00095-5
6. Hussain N, Brull R, Sheehy B, et al. Perineural liposomal bupivacaine is not superior to nonliposomal bupivacaine for peripheral nerve block analgesia. *Anesthesiology*. 2021;134(2):147–164. doi:10.1097/ALN.0000000000003651
7. Sandhu HK, Miller CC, Tanaka A, et al. Effectiveness of standard local anesthetic bupivacaine and liposomal bupivacaine for postoperative pain control in patients undergoing truncal incisions: a randomized clinical trial. *JAMA Network Open*. 2021;4(3):e210753. doi:10.1001/jamanetworkopen.2021.0753
8. Sun S, Yin Q, Shen J, et al. The 90% minimum effective volume and concentration of lidocaine for ultrasound-guided stellate ganglion blocks in adults: a biased-coin design, up-and-down sequential allocation trial. *Kor J Anesthesiol*. 2025;78(5):471–481. doi:10.4097/kja.24607
9. Stylianou M, Flournoy N. Dose finding using the biased coin up-and-down design and isotonic regression. *Biometrics*. 2002;58(1):171–177. doi:10.1111/j.0006-341x.2002.00171.x
10. Fang G, Wan L, Mei W, et al. The minimum effective concentration (MEC90) of ropivacaine for ultrasound-guided supraclavicular brachial plexus block. *Anaesthesia*. 2016;71(6):700–705. doi:10.1111/anae.13445
11. Tsai EH, Nunez-Rodriguez E, Cata JP. Stellate ganglion block in perioperative practice: a narrative review. *Brit J Anaesth*. 2025;136(1):179–196. doi:10.1016/j.bja.2025.07.095
12. Nunez-Rodriguez E, Mishima RS, Martinez F, et al. Stellate ganglion block for preventing perioperative arrhythmias: a systematic review and meta-analysis. *Brit J Anaesth*. 2025. doi:10.1016/j.bja.2025.11.019
13. Xiang XB, Wu YY, Fang Z, et al. Stellate ganglion block for visceral pain in elderly patients undergoing video-assisted thoracoscopic lung cancer surgery: a randomized, controlled trial. *Int J Surg*. 2024;110(11):6996–7002. doi:10.1097/JS9.0000000000001867
14. Shi ZM, Jing JJ, Xue ZJ, et al. Stellate ganglion block ameliorated central post-stroke pain with comorbid anxiety and depression through inhibiting HIF-1α/NLRP3 signaling following thalamic hemorrhagic stroke. *J Neuroinflamm*. 2023;20(1):82. doi:10.1186/s12974-023-02765-2
15. Lee Y, Kim DH, Park J, et al. Stellate ganglion block versus cervical epidural steroid injection for cervical radiculopathy: a comparative-effectiveness study. *Region Anesth Pain M*. 2022. doi:10.1136/rapm-2022-103532
16. Xuan Q, Pan R, Wang A, et al. The 90% minimum effective volume of 0.5 ropivacaine for ultrasound-guided supraclavicular brachial plexus block: a biased coin up-and-down design. *Anaesthesiologie*. 2023;72(Suppl 1):39–43. doi:10.1007/s00101-023-01344-7
17. Plakhotnik J, Zhang L, Estrada M, et al. Local anesthetic cardiac toxicity is mediated by cardiomyocyte calcium dynamics. *Anesthesiology*. 2022;137(6):687–703. doi:10.1097/ALN.0000000000004389
18. Viscusi ER, Sinatra R, Onel E, et al. The safety of liposome bupivacaine, a novel local analgesic formulation. *Clin J Pain*. 2014:30. doi:10.1097/AJP.0b013e318288e1f6.
19. Ilfeld BM. Continuous peripheral nerve blocks: an update of the published evidence and comparison with novel, alternative analgesic modalities. *Anesth Analg*. 2017;124. doi:10.1213/ANE.0000000000001581.
20. Chahar P, Cummings KC. Liposomal bupivacaine: a review of a new bupivacaine formulation. *J Pain Res*. 2012;5:257–264. doi:10.2147/JPR.S27894
21. Hayase J, Vampola S, Ahadian F, et al. Comparative efficacy of stellate ganglion block with bupivacaine vs pulsed radiofrequency in a patient with refractory ventricular arrhythmias. *J Clin Anesth*. 2016. doi:10.1016/j.jclinane.2016.01.026