Open Access Full Text Article

CLINICAL TRIAL REPORT

Minimum Local Anesthetic Dose of Ropivacaine in Cesarean Section for Real-Time Ultrasound-Guided Spinal Anesthesia Using 24-Gauge versus 26-Gauge Needles Based on Fluid Simulation Technology: A Randomized Controlled Trial

Chunying Zheng^{1,*}, Hanliang Fan^{1,*}, Peng Ye^{1,*}, Xing Zhang¹, Xiaochun Zheng^{1,2}, Ting Zheng¹

¹Department of Anesthesiology, Shengli Clinical Medical College of Fujian Medical University, Fujian Provincial Hospital, Fuzhou University Affiliated Provincial Hospital, Fuzhou, People's Republic of China; ²Fujian Provincial Key Laboratory of Emergency Medicine, Fujian Provincial Key Laboratory of Critical Care Medicine, Fujian Provincial Co-Constructed Laboratory of "belt and Road", Fujian Emergency Medical Center, Fuzhou, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xiaochun Zheng; Ting Zheng, Department of Anesthesiology, Shengli Clinical Medical College of Fujian Medical University, No. 134, Dongjie, 350001, Fuzhou, Fujian, People's Republic of China, Tel +86 8821 7841, Email zhengxiaochun7766@163.com; zhengting1223@163.com

Purpose: Previous research has demonstrated that real-time ultrasound-guided (UG) spinal anesthesia requires a higher minimum local anesthetic dose (MLAD) compared to traditional methods. However, the precise MLAD of ropivacaine for UG cesarean sections remains undetermined. In this study, we ascertained the MLAD of ropivacaine for cesarean section. We also investigated the mechanism underlying the diffusion of ropivacaine within the spinal canal using fluid simulation technology.

Patients and Methods: We randomly placed 60 healthy parturients undergoing elective cesarean section with real-time UG spinal anesthesia into Groups I (26-gauge spinal needle) and II (24-gauge spinal needle). For the first parturient in both groups, 15 mg of ropivacaine was administered intrathecally. Based on the effective or ineffective response of the previous parturient, the dose for the subsequent parturient was increased or decreased by 1 mg. Spinal anesthesia characteristics and side effects were recorded. A computer-generated spinal canal model was developed. Leveraging fluid dynamics simulation technology, we documented the diffusion of ropivacaine in the spinal canal using 26-and 24-gauge spinal needles.

Results: The MLADs in Groups I and II were 12.728 mg (12.339–13.130 mg) and 9.795 mg (9.491–10.110 mg), respectively. No significant difference was observed in the onset times and durations of sensory or motor blocks, incidence of complications, or neonatal Apgar scores between both groups. Fluid simulation modeling indicated that the 26-gauge spinal needle achieved a higher distribution level more quickly; however, its peak drug concentration was lower compared to the 24-gauge spinal needle.

Conclusion: For cesarean section anesthetization, the required MLAD of ropivacaine when using a real-time UG 26-gauge spinal needle is significantly greater than that with a 24-gauge needle. The spinal needle diameter influences ropivacaine's MLAD by markedly affecting its diffusion rate within the spinal canal.

Keywords: anesthetic diffusion, spinal needle diameter, fluid dynamics simulation, cesarean anesthetization

Introduction

Globally, approximately 21.1% of women deliver through cesarean section, one of the most common delivery methods.^{1,2} Presently, spinal anesthesia remains the preferred technique for cesarean section.³ Spinal puncture in

parturients is challenging owing to the physiological and pathological changes in these patients. The increasing prevalence of obesity among these women further complicates the procedure. Consequently, the failure rate for spinal puncture in parturients is approximately 20%.^{4,5}

Using ultrasound technology in spinal anesthesia has gained broad acceptance because it enhances intervertebral space localization accuracy and minimizes complications, significantly increasing the safety of spinal anesthesia in obstetric patients.^{6–8} In addition, real-time ultrasound-guided (UG) spinal puncture technology provides a precise depiction of the puncture path relative to surrounding anatomical structures, thereby improving the reliability and safety of the procedure.^{6,9} This approach is especially advantageous for patients undergoing cesarean sections.

Ropivacaine (Naropine[®]; AstraZeneca AB) is a local anesthetic extensively used for spinal anesthesia in parturients.¹⁰ Its minimum local anesthetic dose (MLAD) is crucial for ensuring spinal anesthesia safety. Notably, parturients require lower MLAD than the general population owing to uterine compression on the inferior vena cava, dilation of the epidural venous plexus, increased subarachnoid fat, and decreased cerebrospinal fluid (CSF), which is further affected by biochemical and hormonal changes.¹¹ Consequently, significant research has focused on determining the appropriate MLAD of ropivacaine for parturients.^{12–14} However, research regarding ropivacaine's MLAD for cesarean sections has been primarily directed at traditional spinal anesthesia.^{12,14}

Preliminary studies indicate that the MLAD for ropivacaine with UG spinal anesthesia is notably higher in the general population than with traditional methods. This phenomenon is not fully understood but is speculated to be associated with the precision of interlaminar space localization and the angle of the puncture needle.^{15–17} This variation in MLAD persists in parturients undergoing the same procedure, prompting inquiries about potential MLAD variances from conventional techniques. The appropriate local anesthetic dose is e a critical concern in parturients because of their unique physiological status.¹¹ Consequently, determining the precise MLAD of ropivacaine for UG spinal anesthesia during cesarean sections is essential, offering valuable insights for clinical application.

The specific impact of spinal needle diameter on the anesthetic distribution within the subarachnoid space remains unclear. Ethical restrictions prevent direct patient studies. However, with the increasing application of computational simulation technologies in medicine, fluid dynamics simulations can replicate the drug dispersion process within the spinal canal.¹⁸ This advancement offers a novel approach for studying how needle gauge affects drug distribution in the subarachnoid space. Such technologies hold great promise for future research, enabling us to explore and optimize spinal anesthesia techniques in a simulated environment, thereby overcoming ethical and practical limitations.

In this study, we investigated the impact of needle diameter on the efficacy and spread of drug distribution around the spinal cord by comparing 24- and 26-gauge spinal needles extensively used in spinal anesthesia.¹⁸ Given the difficulty of observing drug dispersion directly in patients' spinal canal, the role of needle size remains conjectural. Our research focuses on determining the MLAD of ropivacaine administered through real-time UG spinal anesthesia with these needle sizes. In addition, it seeks to ascertain the effect of needle diameter on ropivacaine dosage and elucidate the influence of needle size on drug distribution and dispersion within the spinal canal using computational fluid dynamics simulation.

Material and Methods

The Ethics Committee of Fujian Provincial Hospital in Fuzhou, China, approved this study on December 25, 2023 (approval number K2023-12-008) before commencing patient recruitment and sample collection. The study was registered with the Chinese Clinical Trial Registry (registration number ChiCTR2400079509) and adhered to the guidelines of the Declaration of Helsinki. We assessed 65 parturient women (singleton pregnancy; with an American Society of Anesthesiologists (ASA) physical status of II or III; aged 20–45 years; and a gestational period of over 37 weeks) scheduled for elective lower segment cesarean section under real-time UG spinal anesthesia from January to May 2024 for eligibility, and enrolled 60 women. Exclusion criteria encompassed allergies to local anesthetics or nonsteroidal anti-inflammatory drugs, infection at the puncture site, blood coagulation disorders, and specific cardiovas-cular diseases. Participants provided written informed consent and were advised of their right to withdraw at any time. The enrollment data are depicted in Figure 1.

Parturient women were randomly allocated into Groups I (26-gauge spinal needle) and II (24-gauge spinal needle). In this study, randomization was performed using computer-generated random number codes. The study solutions were



Figure I The process of ultrasound-guided real-time intraspinal anesthesia. (A and B) Short-axis in-plane ultrasound technique of anesthesia. (C) Ultrasound images during puncture. (D) The flow of the drug solution resulting from the administration of ropivacaine into the subarachnoid space was observed using color Doppler mode.

prepared by an investigator who was not involved in subsequent anesthetic management or data collection. All parturients fasted for at least 6 h and received no premedication before surgery. Upon arrival in the operating room, all parturients were preloaded with 10 mL/kg lactated Ringer's solution. Electrocardiographic data, pulse oxygen saturation (SPO₂), respiratory rate (RR), heart rate (HR), and blood pressure (BP) were monitored.

Hip flexion and knee clutching in the left lateral position were adopted. Real-time UG intraspinal anesthesia was performed using a commercially available system (Edge II, SonoSite Company) equipped with a 5–10 MHz transducer. The transducer was placed in a paramedian sagittal oblique orientation using sliding and titling scanning techniques to reveal a flat hyperechoic sacrum and locate the L2–3 and L3–4 laminar interspaces.¹⁹ The transducer was rotated 90° in a transverse orientation with respect to the L3–4 laminar interspace, and the needle insertion depth into the anterior complex was measured using the electronic calipers of the ultrasound machine. The operation area was disinfected, and the towels were spread. An aseptic protective sheath was wrapped around the probe, and local anesthesia with 2% lidocaine was administered at the puncture site. Informed by real-time ultrasound images, a 26- or 24-gauge spinal needle (both Quincke) was guided using the short-axis in-plane technique,²⁰ and CSF outflow indicated access to the subarachnoid space (Figure 1). In cases of resorption without blood, the predetermined dose of local anesthetic ropivacaine was diluted with the CSF to achieve a final concentration of 0.5% and packed into a 5-mL syringe. Afterwards, a local anesthetic was injected at 0.4 mL/s with the spinal needle orifice-oriented cephalad. Next, an epidural puncture was performed at the L2–3 interspace with a 16-gauge Tuohy needle, and an epidural catheter was inserted 3–4 cm in the cephalad direction into the epidural space. The patients were placed in the supine position with a 15° head tilt after inducing spinal anesthesia.

According to previous studies, we selected 15 mg as the dose of intrathecal ropivacaine for the first patient in each group.^{21,22} The dose of intrathecal local anesthetic administered to the patients was varied according to Dixon's up-down sequential allocation method. For each subsequent patient, the dose of the study drug was determined by the outcome of the previous patient in the group, with the dosing increment set at 1 mg.²¹ After successful anesthesia, the dose for the next patient was decreased by 1 mg in that group. Conversely, if a failure was recorded, the dose for the next patient was increased by 1 mg in that group. The study defined an effective response as achieving a sensory block of T6 or greater in a pinprick test using a 17-gauge needle within 20 min after injecting the spinal solution. No additional epidural anesthetic or venous analgesia was

needed for intraoperative pain relief.²³ An ineffective response was defined as the failure to reach a bilateral T6 sensory block level within 20 min of administering the drug intrathecally or the need for supplemental epidural/venous analgesia during surgery if the visual analog pain score was >20 mm or the patient requested additional analgesia despite obtaining a T6 sensory level. An epidural anesthetic of 2% lidocaine was added as 5 mL every 10 min as needed.¹⁴ Upon skin closure, patient-controlled intravenous analgesia commenced, utilizing an electronic analgesia pump filled with sufentanil. The protocol included a continuous dose of 2 µg/h, a self-administered dose of 2 µg/h, a 15-min lockout interval, and a maximum dose of 20 µg/h. The epidural catheter was removed after surgery. Hypotension episodes, defined as a systolic BP of <90 mmHg or a decrease of over 20% from the baseline BP, were managed with a 40 µg intravenous bolus of phenylephrine and repeated as necessary. Bradycardia, characterized by an HR of < 50 beats per minute, was treated with 0.5 mg of atropine administered intravenously. Respiratory depression, identified by an SPO₂ level below 90%, was addressed by administering face mask oxygen and additional respiratory support when needed.

Outcome Measures

Two trained anesthesiologists blinded to group assignments meticulously analyzed patients' baseline measurements, encompassing sensory and motor assessments and subsequent data collected post-surgery and throughout the recovery period. The same anesthesiologist performed the spinal anesthesia and the assessments during the anesthesia and surgical procedures.

The level of a sensory block was tested bilaterally with the pinprick test at the midclavicular line and the level of a motor block was assessed with a modified Bromage scale (0 = no motor loss, 1 = inability to flex the hip, 2 = inability to flex the knee, and 3 = inability to flex the ankle). The level of a sensory block was assessed every 2 min within the first 20 min post injection. For cases with ineffective blockade, assessments were continued at 15-min intervals for 1 h post injection following the completion of surgery until normal sensation returned. We recorded the time to achieve a sensory blockade of T6, the maximum spread of sensory blockade, and the duration for sensory blocks higher than T6. The degree of a motor block was assessed at the same time points as the sensory block using the modified Bromage score. Motor block onset time (time taken for the Bromage score to reach 1 point) and duration (time needed to return to 0 points) were recorded.

The Apgar score was recorded 1 and 5 min after the baby was delivered. The frequency of hypotension, nausea, vomiting, respiratory depression (SpO₂<90% or RR<10 breaths/min), uroschesis, epidural hematoma, and nerve injury on the first day after the operation. Postdural puncture headache (PDPH) incidence was monitored on the first, second, third, and seventh postoperative days, with assessments on the final day being conducted through telephone interviews upon patient discharge. A diagnosis of PDPH was established based on the onset of headache worsening within 15 min of sitting or standing and showing improvement within 15 min of reclining. In addition, the presence of at least one of the following symptoms alongside the headache—neck stiffness, tinnitus, hyperacusis, photophobia, or nausea—was necessary for diagnosis, provided the headache appeared within 5 d following the dural puncture.

Sample Size Calculation and Data Analysis

Based on Dixon's up-and-down sequential method, a minimum of 20 patients (six pairs of sequence reversals) are necessary for a stable estimate of MLAD.^{24–26} To account for a 20% dropout rate, each group should have at least 25 patients. As detailed in the flow chart (Figure 2), we enrolled 60 patients (30 in each group).

Statistical analysis and data processing were performed using SPSS 26.0. The normality of continuous data was assessed with Q-Q plots. Quantitative data conforming to a normal distribution were expressed as mean and SD, as appropriate, and analyzed with the Student's *t*-test to identify intergroup differences. Non-normally distributed data were presented as the median (interquartile range) and examined using the Mann–Whitney *U*-test. Categorical variables, such as perioperative adverse reactions and complications, were expressed as numbers (percentages) and evaluated through Pearson's χ^2 or Fisher's exact test. The MLAD and its 95% confidence interval (CI) were determined using Dixon and Massey's sequential method and Probit regression analysis. MLAD and 95% CI comparisons between groups leveraged the formula (Z=(MLAD1-MLAD2) $\div \sqrt{(S1^2+S2^2)}$), where MLAD1 and MLAD2 represent the minimal local anesthetic doses for Groups I and II, respectively, and S1 and S2 are their standard deviations. The comparative concentration spread between both groups was assessed using a paired samples *t*-test. Statistical significance was set at *P*-value < 0.05



Figure 2 A flow diagram showing the process of including participants in the study inclusion.

(two-tailed). Methods and results are reported according to the Consolidated Standards of Reporting Trials Statement (CONSORT).²⁷

Pre-Processing of the Model

Modeling

Based on the actual physiological curvature, the human vertebral canal model was constructed using a real vertebral canal cross-section from human anatomical images. A partial model from L5 to T6 was generated in SpaceClaim software to create solid surfaces and simplify calculations. The inner and outer surfaces were extracted by volume, and the fluid domain was filled. Clinical 24- and 26-gauge puncture needles were used, and the needle tip features were simplified. The injection site was located between the lumbar vertebrae L3–L4 and the characteristic depth of both needle injection ports from the curved surface of the dura mater was approximately 1 mm.

Grid Division

Unstructured polyhedral computational grids in the calculation domain were created by fluent meshing. Grid refinement was carried out near the needle to reduce the occurrence of regions with large gradients. Prism expansion with three layers was applied on the pia mater, dura mater, and needle wall surfaces to meet the needs of laminar viscous flow models. The grid also included the internal needle cavity to enable the calculation of CSF velocity distribution at the needle tip and the initialization of two-phase flow mixing. By reducing grid size and lowering grid precision while meeting the requirements of grid quality, the computational grid that covered all models ultimately consisted of approximately 850,000–900,000 elements.^{28,29}

Submodel Setup

Due to the very small diffusion coefficient of drugs in the CSF, approximately in the order of $10^{10}-10^{11}$ we assumed negligible self-diffusion of drugs in the CSF. Thus, the minor phase, which has a significantly lower content compared to the major phase in the mixing domain, can be analyzed in a large area as a two-phase flow. A simplified Eulerian multiphase flow model, the Mixture Model, was used to simulate an oscillating CSF flow field using a laminar viscous model in ANSYS Fluent software, and drug diffusion was modeled using Fluent Mixture multiphase flow.^{30–32}

Material Property Setup

Major phase: CSF was modeled as an incompressible Newtonian fluid with a viscosity of 0.001 Pas and a density of 998.2 kg/m³, equivalent to water at room temperature. Minor phase: The drug was modeled as a ropivacaine anesthetic, with a density of $1,032 \text{ kg/m}^3$ and a viscosity of 9.795E-4 Pas at room temperature, ignoring the temperature effect on fluid flow.³³

Computer Simulation

The pressure-implicit with splitting of operators format was used for solving the flow equations, second-order upwind discretization for momentum, pressure staging options for pressure discretization, and first-order upwind discretization for volume fraction. The default under-relaxation factor was used. The volume fraction parameters were calculated using an implicit formula, and the dispersed model was used for the phase interface. The convergence criteria for velocity, continuity, momentum, and phase volume fraction were all set to 1E-03. The time step was 0.1 s, and the maximum number of iterations per time step was set at 60, simulating fluid movement within 1200 s after injection.

Simulation Post-Processing

The obtained data was visualized using post-processing software. Source files were rendered into images, animations, and data results.

Results

Figure 2 shows the consort diagram. The baseline characteristics, including age, height, weight, operation time, gestation, and ASA classification, were not significantly different between the groups (P>0.05) (Table 1).

MLAD of Ropivacaine

The MLAD of intrathecal ropivacaine for cesarean section, using the Dixon and Massey up-down sequential method, was 12.728 mg (95% CI, 12.339–13.130 mg) in Group I and 9.795 mg (95% CI, 9.491–10.110 mg) in Group II (Figure 3).

The MLAD of ropivacaine differed significantly between the two groups (P<0.05). When Probit regression was used, the MLAD of intrathecal ropivacaine was 13.034 mg (95% CI, 12.265–13.803 mg) in Group I and 10.291 mg (95% CI, 9.477–11.112 mg) in Group II (Figure 3).

Characteristics	Group I	Group II	Р
Age, y	29.17±3.97	28.60±3.44	0.557
Height, cm	158.67±4.81	158.93±4.58	0.827
Weight, kg	70.87±8.15	68.97±6.77	0.330
BMI, kg/m ²	28.15±3.04	27.35±2.92	0.304
Operation time, min	70.33±11.43	73.33±11.01	0.305
Gestation, days	273.17±5.75	272.40±4.92	0.581
ASA physical status (II/III), n	11/19	10/20	0.788

Table I Baseline Characteristics of Patients in the Two Groups

Notes: Data represent the number of patients or the mean \pm standard deviation. Abbreviation: ASA, American Society of Anesthesiologists.



Figure 3 (A) The 26-gauge spinal needle ultrasound-guided group; (B) the 24-gauge spinal needle ultrasound-guided group. The minimum local anesthetic dose (MLAD) of ropivacaine for cesarean section was 12.728 mg (95% Cl, 12.339–13.130 mg) in Group I and 9.795 mg (95% Cl, 9.491–10.110 mg) in Group II using the formula of Dixon and Massey. The line indicates the MLAD. "=", effective anesthesia; "=", ineffective anesthesia.

Sensory Block in the Two Groups

In Groups I and II, the times to achieve a sensory blockade at the T6 level were 8.533 ± 1.187 min and 8.000 ± 1.414 min, respectively; the maximum spread of sensory blockade was at the T4 (T4–T6) and T3 (T3–T6) level, respectively, and the durations for sensory blocks higher than T6 were 110.000 ± 13.496 min and 111.765 ± 9.176 min, respectively.

The time to achieve a sensory blockade at the T6 level (P=0.261), the maximum spread of sensory blockade (P=0.331), or the duration for sensory blocks higher than T6 (P=0.685) between the two groups did not differ significantly (Table 2).

Motor Block in the Two Groups

In Groups I and II, the onset times for a motor block were 6.533 ± 1.767 min and 6.118 ± 1.495 min, respectively, and the duration of a motor block was 161.000 ± 30.249 min and 154.412 ± 32.156 min, respectively. No statistically significant differences were observed in the onset time (P=0.477) or duration (P=0.557) of a motor block between both groups (Table 2).

Regarding the modified Bromage score, we could not detect any difference at any evaluation time point between both groups (Supplementary Figure S1).

Incidence of Adverse Reactions in the Two Groups

The incidence of postoperative complications did not differ between the two groups (Supplementary Table S1).

Intraspinal Model

A human vertebral canal model was successfully established. A partial model from L5 to T6 was generated in SpaceClaim software to create solid surfaces; the inner and outer surfaces were extracted by volume, and the fluid domain was filled (Supplementary Figure S2).

Variable	Group I	Group II	Р
Sensory block (min)			
Reached time of T6	8.533±1.187	8.000±1.414	0.261
Duration of time above T6	110.000±13.496	111.765±9.176	0.685
The highest plane	T4 (T4-T6)	T3 (T3-T6)	0.331
Motor block (min)			
Onset time	6.533±1.767	6.118±1.495	0.477
Duration	161.000±30.249	154.412±32.156	0.557

Notes: No statistical significance was observed between groups. Data are presented as the mean \pm SD.

Variations in Drug Concentration on Different Planes

The rate of drug concentration increased faster at the T10, T11, and T12 cross-sections with the 26-gauge thin needle than with the 24-gauge thicker needle. This may be related to a faster drug flow rate with thin needles (Figure 4). However, compared with the 24-gauge needle, the drug concentration with the 26-gauge needle peaked quickly before



Figure 4 Drug concentration variation diagrams on different planes. (A) shows the diffusion of ropivacaine in the spinal canal through a 24-gauge needle after 600 seconds. This diagram highlights how the anesthetic spreads within the subarachnoid space, depicting varying concentrations distributed across different regions; (B) ropivacaine diffusion using a 26-gauge needle at the same interval; (C–E) display the transitions in intrathecal ropivacaine levels within the T10–T12 vertebral segment over a longer duration of 1200 s.

rapidly declining, and the subsequent drug concentrations at the T10, T11, and T12 cross-sections were lower than those with the thick needle. The effective concentration at the target plane was higher with the 24-gauge needle.

Discussion

In this prospective randomized study, which employed an up-and-down sequential allocation, we found that using 26and 24-gauge spinal needles in UG spinal anesthesia yielded effective results without an increased risk of complications. Notably, the MLAD required for the 26-gauge needle, averaging 12.728 mg (95% CI, 12.339–13.130 mg), was significantly higher than the 9.795 mg (95% CI, 9.491–10.110 mg) required for the 24-gauge needle (P<0.05), suggesting that needle diameter plays a critical role in determining the MLAD.

Ciftci et al³⁴ proposed that needle diameter size indirectly influences ropivacaine's MLAD by altering local anesthetic flow rate, diffusion characteristics within the spinal canal, and potentially CSF dynamics. Specifically, a narrower spinal needle increases the local anesthetic's flow rate under uniform injection pressure, potentially altering its diffusion within the spinal canal.¹⁸ Conversely, a reduced flow rate achieves a stable laminar flow in the CSF, promoting an even drug distribution for more effective anesthesia. In contrast, a needle with a smaller diameter may increase solution flow rate, elevate turbulence risk, lead to uneven local anesthetic distribution in the subarachnoid space, create irregular concentration gradients, and thus enhance variability in anesthesia effect.

Building an intrathecal model and utilizing fluid simulation technology to study the dispersion of anesthetic agents within the spinal canal is innovative and significant. This approach replicates the drug distribution process by leveraging advanced computational simulations. This is particularly valuable given the ethical and practical limitations of direct studies in patients. By modeling the spinal canal and simulating fluid dynamics, we can understand how different factors, such as needle gauge and injection speed, affect the distribution of anesthetic agents. This study innovatively employed fluid simulation technology,³⁵ revealing for the first time the diffusion dynamics of ropivacaine within the spinal canal using two different sizes of lumbar puncture needles. The simulation results indicate that the 26-gauge spinal anesthesia needle reached a higher drug concentration more rapidly than the 24-gauge needle at the T10, T11, and T12 sections, likely due to the faster flow rate of medication injected by the finer needle. However, with the 26-gauge needle, the drug levels declined swiftly after reaching peak concentrations compared to the 24-gauge needle, resulting in lower concentrations at subsequent T10, T11, and T12 sections. The 24-gauge spinal anesthesia needle maintains a higher effective concentration at the target planes. This explains why the MLAD required with the 26-gauge needle under UG spinal anesthesia is higher than that of the 24-gauge in this study.

Liu et al¹⁵ and our initial findings indicate that for lower limb surgeries within the general population, using UG single spinal anesthesia requires a higher MLAD for bupivacaine and ropivacaine compared to the traditional method.^{16,17} For instance, the MLAD for 0.5% ropivacaine reached 20.192 mg in knee surgeries employing ultrasound guidance, as opposed to 17.176 mg required under the conventional approach.¹⁷ Contrary to these findings, our study recorded MLADs of 12.728 mg and 9.795 mg for the 26- and 24-gauge needles, respectively. This is approximately consistent with previous studies.^{12–14,36,37} Tang et al,¹⁴ used the Dixon sequential method and Probit regression analysis and found that the 50% effective doses (ED50s) of ropivacaine were 11.4 and 11.1 mg, respectively, when using a 27-gauge spinal needle for spinal anesthesia at the L3–4 interspace during cesarean sections. Similarly, Mei et al¹³ also used Probit regression analysis and found that the ED50 of ropivacaine was 11.2 mg with a 26-gauge spinal needle. This discrepancy could be attributed to the precise identification of the intervertebral space through ultrasound, minimizing the risk of puncture point deviation. In addition, the sensitivity to local anesthetics may be amplified in late-stage pregnant women due to anatomical and hormonal alterations, possibly influencing these outcomes.¹¹

In this study, the durations required to achieve the T6 level following spinal anesthesia were 8.533 ± 1.187 min and 8.000 ± 1.414 min for the respective groups. These findings reveal a quicker onset compared to our prior study, where reaching the T10 level post-UG spinal anesthesia in a general cohort necessitated 16.714 ± 1.790 min. In addition, the sensory blockade durations surpassing the T6 plane were 110.000 ± 13.496 min and 111.765 ± 9.176 min, exceeding the sensory blockade duration above the T10 plane reported in our earlier research (90.143 ± 13.163 min),¹⁷ corroborating the heightened sensitivity of parturients to local anesthetics.

No significant differences were observed between the two groups regarding the incidence of hypotension, nausea, vomiting, respiratory depression, and bradycardia. In addition, the Apgar scores of newborns at the 1st and 5th min

showed no significant variations between the groups. The absence of any newborns with an Apgar score below 8 further demonstrates the safety of employing real-time UG spinal anesthesia in cesarean deliveries.

Applying fluid simulation technology allowed us to simulate the diffusion process of ropivacaine in the spinal canal using two different sizes of lumbar puncture needles. The simulation results revealed that when using the fine 26-gauge needle, the drug concentration rapidly decreased after reaching its peak, and the drug concentration at the T10, T11, and T12 cross-sections was generally lower than when using the thicker 24-gauge needle. This explains why the MLAD required for the 24-gauge needle is lower than that for the 26-gauge needle when reaching the same block plane.

This study had some limitations. Primarily, constraints on computational resources precluded the simulation of how various puncture angles and changes in patient positioning might influence anesthetic solution diffusion, an aspect intended for future research. In addition, the ED95 for ropivacaine, a measure with significant clinical relevance, is yet to be explored in this research.

Future research will continue to leverage the intrathecal model and fluid simulation technology to explore various aspects of spinal anesthesia. One promising area of investigation is the impact of different puncture angles on the distribution of anesthetic agents within the spinal canal. By simulating these variations, we hope to optimize puncture techniques to enhance the efficacy and safety of spinal anesthesia. This will involve computational simulations and corroborative studies to validate the findings. These advancements will contribute to a deeper understanding of how to best administer spinal anesthesia, ultimately improving clinical practices and patient care.

Conclusion

This research illustrates that for cesarean section anesthetization, the required MLAD of ropivacaine when applied using a 26-gauge spinal needle under real-time UG is significantly greater than with a 24-gauge needle. The diameter of the spinal needle plays a crucial role in determining ropivacaine's MLAD by markedly affecting the rate of diffusion of the anesthetic within the spinal canal.

Abbreviations

ASA, American Society of Anesthesiologists; BP, blood pressure; CSF, cerebrospinal fluid, CONSORT, consolidated standards of reporting treatment statements; ED, effective dose; HR, heart rate; UG, ultrasound-guided.

Data Sharing Statement

All data generated or analyzed during this study were included in the published article. Further inquiries about the datasets can be directed to the corresponding author on reasonable request.

Funding

This research was funded by a grant from Startup Fund for Scientific Research, Fujian Medical University (Grant number: 2021QH1317); the Joint Funds for the Innovation of Science and Technology of Fujian Province (No. 2023Y9282); Enze Medical Research Projects for Pain Management (Grant number: ezmr2022-005); Fujian provincial health technology project (Grant numbers: 2023CXA007) and the Natural Science Foundation of Fujian Province (Grant number: 2023J011194). The authors report no involvement of the sponsor in the research, which could have influenced the outcome of this study.

Disclosure

The authors report no conflicts of interest in this work.

References

- 1. Betran AP, Ye J, Moller AB, Souza JP, Zhang J. Trends and projections of caesarean section rates: global and regional estimates. *BMJ Glob Health*. 2021; 6:e005671.
- Qiao J, Wang Y, Li X, et al. A Lancet Commission on 70 years of women's reproductive, maternal, newborn, child, and adolescent health in China. Lancet. 2021;397:2497–2536. doi:10.1016/S0140-6736(20)32708-2

- Practice guidelines for obstetric anesthesia: an updated report by the American society of anesthesiologists task force on obstetric anesthesia and the Society for Obstetric Anesthesia and Perinatology. Anesthesiology. 2016;124:270–300. doi:10.1097/ALN.00000000000935
- Harrison DA, Langham BT. Spinal anaesthesia for urological surgery. A survey of failure rate, postdural puncture headache and patient satisfaction. Anaesthesia. 1992;47:902–903. doi:10.1111/j.1365-2044.1992.tb03161.x
- Kazma JM, van den Anker J, Allegaert K, Dallmann A, Ahmadzia HK. Anatomical and physiological alterations of pregnancy. J Pharmacokinet Pharmacodyn. 2020;47:271–285. doi:10.1007/s10928-020-09677-1
- Elsharkawy H, Maheshwari A, Babazade R, Perlas A, Zaky S, Mounir-Soliman L. Real-time ultrasound-guided spinal anesthesia in patients with predicted difficult anatomy. *Minerva Anestesiol*. 2017;83:465–473. doi:10.23736/S0375-9393.16.11610-4
- 7. Kim S, Adler DK. Ultrasound-assisted lumbar puncture in pediatric emergency medicine. J Emerg Med. 2014;47:59-64. doi:10.1016/j. jemermed.2012.09.149
- 8. Creanga AA, Catalano PM, Bateman BT, Longo DL. Obesity in pregnancy. N Engl J Med. 2022;387:248-259. doi:10.1056/NEJMra1801040
- Chong SE, Mohd Nikman A, Saedah A, et al. Real-time ultrasound-guided paramedian spinal anaesthesia: evaluation of the efficacy and the success rate of single needle pass. Br J Anaesth. 2017;118:799–801. doi:10.1093/bja/aex108
- 10. Simpson D, Curran MP, Oldfield V, Keating GM. Ropivacaine: a review of its use in regional anaesthesia and acute pain management. *Drugs*. 2005;65:2675–2717. doi:10.2165/00003495-200565180-00013
- 11. Suresh M, Preston RL, Fernando R, et al. Shnider and Levinson's Anesthesia for Obstetrics. Lippincott Williams & Wilkins; 2012.
- 12. Lv M, Zhang P, Wang Z. ED50 of intrathecal ropivacaine for cesarean delivery with and without epidural volume extension with normal saline: a randomized controlled study. *J Pain Res.* 2018;11:2791–2796. doi:10.2147/JPR.S174176
- 13. Mei Z, Ngan Kee WD, Sheng ZM, et al. Comparative dose-response study of hyperbaric ropivacaine for spinal anesthesia for cesarean delivery in singleton versus twin pregnancies. J Clin Anesth. 2020;67:110068. doi:10.1016/j.jclinane.2020.110068
- 14. Tang Y, Yang M, Fu F, Huang X, Feng Y, Chen X. Comparison of the ED50 of intrathecal hyperbaric ropivacaine co-administered with or without intrathecal dexmedetomidine for cesarean section: a prospective, double-blinded, randomized dose-response trial using up-down sequential allocation method. J Clin Anesth. 2020;62:109725. doi:10.1016/j.jclinane.2020.109725
- 15. Liu Y, Yang S, Yao W, et al. Minimum effective dose of plain bupivacaine 0.5% for ultrasound-guided spinal anaesthesia using Taylor's approach. *Br J Anaesth.* 2020;124:e230–e231. doi:10.1016/j.bja.2020.03.008
- 16. Zheng T, Ye P, Wu W, et al. Minimum local anesthetic dose of ropivacaine in real-time ultrasound-guided intraspinal anesthesia for lower extremity surgery: a randomized controlled trial. *Ann Transl Med.* 2020;8:861. doi:10.21037/atm-20-3805
- 17. Zheng T, Zheng CY, Yan LP, et al. Comparing the minimum local anesthetic dose of ropivacaine in real-time ultrasound-guided spinal anesthesia and traditional landmark-guided spinal anesthesia: a randomized controlled trial of knee surgery patients. *Ann Transl Med.* 2021;9:1492. doi:10.21037/atm-21-3888
- 18. Hocking G, Wildsmith JA. Intrathecal drug spread. Br J Anaesth. 2004;93:568-578. doi:10.1093/bja/aeh204
- 19. Chin KJ, Karmakar MK, Peng P, Warner DS. Ultrasonography of the adult thoracic and lumbar spine for central neuraxial blockade. *Anesthesiology*. 2011;114:1459–1485. doi:10.1097/ALN.0b013e318210f9f8
- 20. Liu Y, Qian W, Ke XJ, Mei W. Real-time ultrasound-guided spinal anesthesia using a new paramedian transverse approach. *Curr Med Sci.* 2018;38:910–913. doi:10.1007/s11596-018-1961-7
- Geng ZY, Wang DX, Wu XM. Minimum effective local anesthetic dose of intrathecal hyperbaric ropivacaine and bupivacaine for cesarean section. *Chin Med J.* 2011;124:509–513.
- Michalek-Sauberer A, Kozek-Langenecker SA, Heinzl H, Deusch E, Chiari A. Median effective local anesthetic doses of plain bupivacaine and ropivacaine for spinal anesthesia administered via a spinal catheter for brachytherapy of the lower abdomen. *Reg Anesth Pain Med.* 2008;33:4–9. doi:10.1097/00115550-200801000-00002
- 23. Dixon WJ. Staircase bioassay: the up-and-down method. Neurosci Biobehav Rev. 1991;15:47-50. doi:10.1016/S0149-7634(05)80090-9
- 24. DW J. The up-and-down method for small samples. J Am Stat Assoc. 1965;967-978.
- Oron AP, Souter MJ, Flournoy N. Understanding research methods: up-and-down designs for dose-finding. Anesthesiology. 2022;137:137–150. doi:10.1097/ALN.000000000004282
- Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Int J Surg.* 2012;10:28–55. doi:10.1016/j.ijsu.2011.10.001
- Clarke EC, Fletcher DF, Stoodley MA, Bilston LE. Computational fluid dynamics modelling of cerebrospinal fluid pressure in Chiari malformation and syringomyelia. J Biomech. 2013;46:1801–1809. doi:10.1016/j.jbiomech.2013.05.013
- Hettiarachchi HDM, Hsu Y, Harris TJ, Penn R, Linninger AA. The effect of pulsatile flow on intrathecal drug delivery in the spinal canal. Ann Biomed Eng. 2011;39:2592–2602. doi:10.1007/s10439-011-0346-x
- 29. Gholampour S, Fatouraee N, Seddighi AS, Seddighi A. Numerical simulation of cerebrospinal fluid hydrodynamics in the healing process of hydrocephalus patients. J Appl Mech Tech Phy. 2017;58:386–391. doi:10.1134/S0021894417030026
- 30. Helgeland A, Mardal K-A, Haughton V, Reif BAP. Numerical simulations of the pulsating flow of cerebrospinal fluid flow in the cervical spinal canal of a Chiari patient. *J Biomech.* 2014;47:1082–1090. doi:10.1016/j.jbiomech.2013.12.023
- Cheng S, Stoodley MA, Wong J, Hemley S, Fletcher DF, Bilston LE. The presence of arachnoiditis affects the characteristics of CSF flow in the spinal subarachnoid space: a modelling study. J Biomech. 2012;45(7):1186–1191. doi:10.1016/j.jbiomech.2012.01.050
- 32. Nógrádi A, Haga PT, Pizzichelli G, et al. A numerical investigation of intrathecal isobaric drug dispersion within the cervical subarachnoid space. *PLoS One.* 2017; 12:e0173680.
- 33. Ciftei T, Daskaya H, Efe S. Comparing spinal blockade effectiveness and maternal hemodynamics using 25 gauge and 29 gauge spinal needles with the same volumetric flow rate in patients undergoing caesarean section. J Obstet Gynaecol. 2017;37:719–722. doi:10.1080/01443615.2017.1290055
- 34. Zhan W, Martin BA, Kalata W, et al. Hydrodynamic and longitudinal impedance analysis of cerebrospinal fluid dynamics at the craniovertebral junction in Type I Chiari malformation. *PLoS One.* 2013; 8:e75335.
- 35. Chapron K, Sleth JC, Capdevila X, Bringuier S, Dadure C. Hyperbaric prilocaine vs. hyperbaric bupivacaine for spinal anaesthesia in women undergoing elective caesarean section: a comparative randomised double-blind study. *Anaesthesia*. 2021;76:777–784. doi:10.1111/anae.15342

36. Chen X, Qian X, Fu F, Lu H, Bein B. Intrathecal sufentanil decreases the median effective dose (ED50) of intrathecal hyperbaric ropivacaine for caesarean delivery. *Acta Anaesthesiol Scand.* 2010;54:284–290. doi:10.1111/j.1399-6576.2009.02051.x

37. Hsu Y, Hettiarachchi HDM, Zhu DC, Linninger AA. The frequency and magnitude of cerebrospinal fluid pulsations influence intrathecal drug distribution: key factors for interpatient variability. Anesth Analg. 2012;115:386–394. doi:10.1213/ANE.0b013e3182536211

Drug Design, Development and Therapy



Publish your work in this journal

Drug Design, Development and Therapy is an international, peer-reviewed open-access journal that spans the spectrum of drug design and development through to clinical applications. Clinical outcomes, patient safety, and programs for the development and effective, safe, and sustained use of medicines are a feature of the journal, which has also been accepted for indexing on PubMed Central. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/drug-design-development-and-therapy-journal