

Levobupivacaine concentration for the ultrasound-guided rectus sheath block in children undergoing umbilical skin incision: An up-and-down dose-finding study

INTRODUCTION

Levobupivacaine, a long-acting local anaesthetic, is equally efficacious as bupivacaine but has a superior pharmacokinetic profile. Rectus sheath block (RSB) can provide superior peri-operative analgesia for paediatric navel skin incisions, such as laparoscopic surgery or umbilical hernia repair.^[1,2] However, the bilateral nature of RSB can cause local anaesthetic toxicity influenced by drug concentration and volume. Ultrasound-guided RSB is widely used in post-operative analgesia; however, the optimal dose of local anaesthetics for the technique is not standardised. This study aimed to determine the optimal levobupivacaine concentration for ultrasound-guided RSB in paediatric patients.

METHODS

The study was carried out according to the principles of the Declaration of Helsinki, 2013. Ethics committee approval was obtained from the Review Board of Human Experiments and the University of Tsukuba Ethics Committee (Tsukuba Clinical Research and Development Organization, vide approval number H24-047). The trial was registered in the University Hospital Medical Information Network Centre Clinical Trials Register (Registration number: UMIN000042702; https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000048734).

In total, 23 paediatric patients aged 1–10 years, with American Society of Anesthesiologists physical status (ASA-PS) I or II, with written informed consent from their parents, were enrolled to determine the optimal levobupivacaine concentration for ultrasound-guided RSB. Patients with contraindications to RSB, allergies to local anaesthetics, lack of parental consent, and those requiring more than 3 mg/kg of levobupivacaine were excluded.

In the operating room, patients received general anaesthesia by administration of oxygen mixed with sevoflurane via a mask of the child's or parent's choice (e.g., vanilla, chocolate, or fruit) as the child fell asleep. Monitoring included pulse oximetry, electrocardiography, and non-invasive blood pressure without premedication. Peripheral venous access was established. Tracheal intubation with a Macintosh laryngoscope under 5% sevoflurane without narcotic analgesics or neuromuscular blocking drugs was followed by maintenance anaesthesia with 2% sevoflurane end-tidal concentration of sevoflurane, oxygen, and air (fraction of inspired oxygen, 0.4) (approximately 1 minimum alveolar concentration (MAC). Volume-controlled ventilation with a tidal volume of 6–8 mL/kg or pressure-controlled ventilation was adjusted to maintain end-tidal carbon dioxide as 35–45 mmHg.

After general anaesthesia induction, ultrasound-guided RSB (S-Nerve unit, Sonosite, Bothell, WA) using a 6–13 MHz linear probe (HFL 38X) and a 25-G 22-mm needle (B. Braun, Melsungen, Germany) was administered. The probe was placed perpendicular to the cephalocaudal orientation of the rectus abdominis muscle fibres, and the block needle was inserted parallel to the muscle's lateral third under ultrasound guidance. After confirming negative aspiration, 3 mL levobupivacaine was injected on both sides. Procedures were performed by resident anaesthesiologists with <5 years of experience. The initial concentration was 0.5%, adjusted by $\pm 0.05\%$ using Dixon's up-and-down method.^[3-6] Surgeries began ≥ 15 minutes post RSB. No body movement during skin incision and <20% haemodynamic changes compared to pre-incision levels in 5 min indicated a 'complete block'. Fentanyl was given as needed at the discretion of the anaesthetist-in-charge after post-block assessment for peritoneal traction or pneumoperitoneum pain.

With reference to previous studies, six 'failure-complete' pairs were needed to obtain 80% statistical power ($1 - \beta = 0.80$) and a two-sided alpha level of 0.05 ($\alpha = 0.05$).^[5,6] Data sampling until at least six pairs were required. Data were presented as mean (standard deviation). Logistic analysis was performed to calculate the minimum effective local anaesthetic concentration in 50% of patients (ED_{50}), minimum effective local anaesthetic concentration in 95% of patients (ED_{95}), and 95% confidence interval (CI) (SAS System, version 6.12, SAS Institute Inc., Cary, NC).

RESULTS

In total, 23 patients were enrolled in this study, with no need for exclusions, for planned levobupivacaine doses of ≥ 3 mg/kg. The study included 23 patients, 8 males and 15 females, 49.6 (28) months of age, 97.8 (18) cm in height, and 15.1 (5) kg in weight. All patients had ASA-PS of I or II. Three patients underwent umbilicoplasty, while the rest underwent laparoscopic inguinal hernia repair. The highest levobupivacaine concentration used was 0.5%. Figure 1 shows the RSB's complete success rate for each levobupivacaine concentration change via the up-and-down method. Figure 2 shows the dose-response curve for levobupivacaine concentration and RSB complete success rate. The analysis indicated an ED_{50} of 0.17% (CI -0.29%, 0.25%) and an ED_{95} of 0.35% (CI 0.26%, 2.93%). Levobupivacaine concentrations of 0.3% or higher provided sufficient analgesia without incisional pain stimulation. No signs of local anaesthesia toxicity, such as new arrhythmias, post-operative convulsions, or altered consciousness, were observed. No other RSB-related complications occurred, such as unexpected bleeding, haematoma, or gastrointestinal perforation.

DISCUSSION

We observed that 0.35% levobupivacaine could provide optimal analgesia for ultrasound-guided RSB in paediatric patients.

A meta-analysis suggested that the optimal concentration of ropivacaine for postoperative analgesia in children is 0.25%.^[7] The comparative potency of ropivacaine and levobupivacaine in paediatric peripheral nerve blockade remains inconclusive, though levobupivacaine is believed to be equally potent.^[8] Patients undergoing umbilical hernia surgery received RSB with 0.25% levobupivacaine

without requiring additional analgesics or experiencing increased heart rate and blood pressure during incision.^[9] However, that study used nitrous oxide, which has analgesic effects. To evaluate the analgesic efficacy of RSB, we did not utilise any narcotic analgesics, nitrous oxide, or premedication. Therefore, higher anaesthetic concentrations may be necessary for surgical procedures when relying solely on RSB analgesia.

The success of peripheral nerve blocks depends on the concentration and volume of the local anaesthetic.^[10] For simplification, we maintained a constant volume of anaesthetic and focused on determining the optimal concentration required for a successful RSB. In future, we plan to investigate the necessary volume of local anaesthetic for RSB.

Because we used ultrasound guidance, 3 mL of local anaesthetic effectively covered the umbilicus area. One study reported that 0.7 mL of local anaesthetic was sufficient to block the ulnar nerve in adults with an average thickness of 6.2 mm²; however, paediatric cutaneous nerves are thinner.^[11] In a previous study on ilioinguinal nerve blocks, abdominal cutaneous nerves in children were effectively blocked with 3 mL anaesthetic.^[5] Another study demonstrated effective RSBs with bilateral administration of 0.1 mL/kg levobupivacaine.^[9] The RSB involves injecting and filling the area where the nerve should be rather than identifying and surrounding the nerve with local anaesthetic. To ensure adequate dosage and eliminate block failure, we standardised the dose to 3 mL per side, totalling 6 mL, suitable even for our study's heaviest child (27 kg). Excessive local anaesthesia poses risks, and the maximum safe dose of ropivacaine

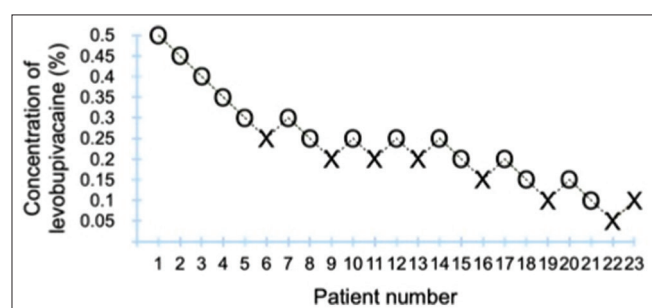


Figure 1: Sequential response of 23 children to the initial incision following changes in the anaesthetic concentration using the up-and-down method. × = failed block; ○ = complete block

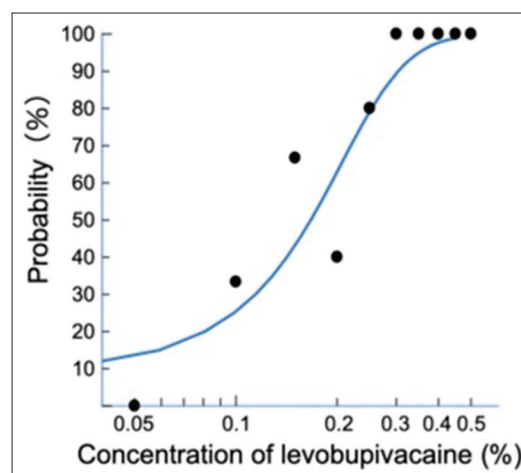


Figure 2: Dose-response curve for levobupivacaine concentration

in paediatric patients is 3 mg/kg.^[12] A study reported no difference in neurotoxicity and cardiac toxicity between ropivacaine and levobupivacaine.^[13] If the use of 6 mL of the planned concentration of the drug would have resulted in a dose exceeding 3 mg/kg, the patient would have been excluded from the study. However, no such cases were encountered during the study. The maximum dose of levobupivacaine needed in our study was 3 mg/kg.

Our study has some limitations. Non-blinded investigators performed the RSB procedure and efficacy assessment. We used a consistent sevoflurane concentration regardless of age, potentially leading to some children being unresponsive to umbilical skin incision pain. The experience level of operators, determined by the number of procedures performed, was unspecified. Due to short hospital stays, post-operative analgesia could not be evaluated comprehensively. For post-operative analgesia alone, a lower levobupivacaine concentration might suffice.

CONCLUSION

A 0.35% levobupivacaine concentration was necessary for analgesia with ultrasound-guided RSB in paediatric patients undergoing umbilical skin incisions under general anaesthesia.

Study data availability

De-identified data may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared after approval as per the authors' institutional policy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

ORCID

Yoshiyuki Hiramoto: <https://orcid.org/0000-0002-2579-2863>

Shinichi Inomata: <https://orcid.org/0000-0002-9283-5026>

Makoto Tanaka: <https://orcid.org/0000-0001-5545-3443>

**Yoshiyuki Hiramoto^{1,2}, Shinichi Inomata³,
Makoto Tanaka³**

¹Department of Anesthesiology and Pain Medicine, Juntendo University Urayasu Hospital, Urayasu, Chiba, ²Department of Anesthesiology, University of Tsukuba Hospital, ³Department of Anesthesiology, Division of Clinical Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

Address for correspondence:

Dr. Shinichi Inomata,
Department of Anesthesiology, Division of Clinical Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba City, Ibaraki, Japan.
E-mail: inomatas@md.tsukuba.ac.jp

Submitted: 01-Jun-2023

Revised: 05-Dec-2023

Accepted: 13-Dec-2023

Published: 29-Jan-2024

REFERENCES

- Chen L, Liu S, Cao Y, Yan L, Shen Y. Rectus sheath block versus local anaesthetic infiltration in pediatric laparoscopic inguinal hernia repair: A randomized controlled trial. *Int J Surg* 2023;109:716-22.
- Flack SH, Martin LD, Walker BJ, Bosenberg AT, Helmers LD, Goldin AB, *et al.* Ultrasound-guided rectus sheath block or wound infiltration in children: A randomized blinded study of analgesia and bupivacaine absorption. *Pediatr Anesth* 2014;24:968-73.
- Dixon WJ. Staircase bioassay: The up-and-down method. *Neurosci Biobehav Rev* 1991;15:47-50.
- Johnston DF, Sondekoppam RV, Giffin R, Litchfield R, Ganapathy S. Determination of ED₅₀ and ED₉₅ of 0.5% ropivacaine in adductor canal block to produce quadriceps weakness: A dose-finding study. *Reg Anesth Pain Med* 2017;42:731-6.
- Yamada K, Inomata S, Tanaka M. The ropivacaine concentration required for ultrasound-guided ilioinguinal/iliohypogastric nerve block in pediatric patients. *Anesth Analg* 2016;123:175-8.
- Sebel PS, Glass PSA, Fletcher JE, Murphy MR, Gallagher C, Quill T. Reduction of the MAC of desflurane with fentanyl. *Anesthesiology* 1992;76:52-9.
- Winnie L, Kao YH, Liao CC, Tamura T, Chang ML, Hsieh KY. Comparative analgesic efficacies of ropivacaine and bupivacaine for postoperative rectus sheath block in paediatric abdominal surgery: A meta-analysis of randomised controlled trial and retrospective cohort studies. *Pain Res Mana* 2021;2021:5535730. doi: 10.1155/2021/5535730.
- Li A, Wei Z, Liu Y, Shi J, Ding H, Tang H, *et al.* Ropivacaine versus levobupivacaine in peripheral nerve block: A PRISMA-compliant meta-analysis of randomized controlled trials. *Medicine (Baltimore)* 2017;96:e6551. doi: 10.1097/MD.0000000000006551.
- Willschke H, Bösenberg A, Marhofer P, Johnston S, Kettner SC, Wanzel O, *et al.* Ultrasonography-guided rectus sheath block in paediatric anaesthesia—a new approach to an old technique. *Br J Anaesth* 2006;97:244-9.
- Fredrickson MJ, Smith KR, Wong AC. Importance of volume and concentration for ropivacaine interscalene block in preventing recovery room pain and minimizing motor block after shoulder surgery. *Anesthesiology* 2010;112:1374-81.
- Eichenberger U, Stöckli S, Marhofer P, Huber G, Willmann P, Kettner SC, *et al.* Minimal local anesthetic volume for peripheral nerve block: A new ultrasound-guided, nerve dimension-based method. *Reg Anesth Pain Med* 2009;34:242-6.
- Dalens B, Ecoffey C, Joly A, Giafré E, Gustafsson U, Huledal G, *et al.* Pharmacokinetics and analgesic effect of ropivacaine

following ilioinguinal/iliohypogastric nerve block in children. *Pediatr Anesth* 2001;11:415-20.

13. Stewart J, Kellett N, Castro D. The central nervous system and cardiovascular effects of levobupivacaine and ropivacaine in healthy volunteers. *Anesth Analg* 2003;97:412-6.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online

Quick response code



Website:
<https://journals.lww.com/ijaweb>

DOI:
10.4103/ija.ija_514_23

How to cite this article: Hiramoto Y, Inomata S, Tanaka M. Levobupivacaine concentration for the ultrasound-guided rectus sheath block in children undergoing umbilical skin incision: An up-and-down dose-finding study. *Indian J Anaesth* 2024;68:196-9.