



The median effective concentration of ropivacaine for ultrasound-guided caudal block in children: a dose-finding study

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Abstract

Purpose To determine the 50% minimum effective concentration (MEC50) and the 95% effective concentration (MEC95) of ropivacaine for ultrasound-guided caudal block during hypospadias repair surgery of pediatric patients.

Methods Children were enrolled with the American Society of Anesthesiologists (ASA) physical status I–II undergoing elective hypospadias repair surgery. Children were grouped into two age groups: toddlerhood (1–3 years old) and preschool (3–6 years old). We measured The MEC50 using Dixon's up-and-down method. The first children received the caudal block with 1.0 mL/kg of 0.15% ropivacaine. We determined each subsequent patient's concentration based on the previous patient's response and adjusted the concentration in intervals of 0.015%. Meanwhile, the probit regression analysis obtains 95% effective concentration (MEC95). In addition, we recorded the general condition, adverse events, and postoperative pain of each child.

Results 46 children undergoing elective hypospadias repair surgery were included in this study, 22 in the toddlerhood group and 24 in the preschool group. Of the total number of patients, the caudal block was successful in 25 (54%) and failed in 21 (46%). The MEC50 of 1 ml/kg ropivacaine was 0.102% (95% CI 0.099%, 0.138%) in the toddlerhood group and 0.129% (95% CI 0.124%, 0.138%) in the preschool group. The MEC95 of 1 ml/kg ropivacaine was 0.148% (95% CI 0.131%, 0.149%) in the toddlerhood group and 0.162% (95% CI 0.134%, 0.164%) in the preschool group. Our results showed that ropivacaine concentration was statistically different between preschool children and toddlers ($P < 0.001$). None of the adverse events occurred.

Conclusions This study showed that children in the preschool group required higher concentrations of ropivacaine than children in the toddler group during ultrasound-guided sacral block combined with non-intubated general anesthesia. At the same time, this method of anesthesia is safe and effective for children undergoing surgery for hypospadias.

Keywords Caudal block · Ropivacaine · Child · Hypospadias · MEC₅₀

Introduction

Ropivacaine (Naropin[®], AstraZeneca) is an amide-type and long-acting regional anesthetic with lower central nervous and cardiac toxic potential than other local anesthetic agents [1]. Available data show ropivacaine to be very suitable for regional anesthesia [2].

Hypospadias is one of the most common severe conditions of male children's genitals, and the incidence of it is approximately (0.2–4.1)/1000 in live births [3]. Caudal block can provide a satisfactory analgesic effect for hypospadias repair surgery [4].

A previous study suggested that a caudal block with high volume/low concentration ropivacaine provides a longer analgesic duration after discharge than low volume/high

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concentration ropivacaine in children [5]. A study revealed that the adequate volume reaching the L2 vertebral level of the caudal block was at least 1 ml/kg in children aged 1–7 years [6]. Another study showed that when 1 ml/kg local anesthetic was used to perform sacral block in children, the block plane could basically reach the L1–L2 level, and the maximum block level could reach T10 [7]. But so far, the ropivacaine concentration was not clear enough for children of different ages.

Therefore, we divided the research subjects into two age groups: 1–3 years old and 3–6 years old, to measure the minimum concentration of ropivacaine to provide scientific reference for pediatric medication.

Materials and methods

Ethical approval was obtained from the Institutional Review Board of the Children's Hospital of Chongqing Medical University in 2020 (No. 140-2). Before enrollment, this prospective clinical trial was registered on chictr.org.cn (ChiCTR2200057902; principal investigator: H.C.; registration date: March 22, 2022). Parents/guardians of all patients informed consent and signed the consent form. From March 2022 to December 2022, Patients aged 1 and 6 years with an ASA physical status I or II who were scheduled for hypospadias repair surgery were considered for inclusion. There were several criteria for exclusion from the study, including lack of consent, a known history of ropivacaine allergy, sacral tail deformity, infection at the puncture site, neurological or neuromuscular disease, blood clotting disorders, or any systemic severe disease.

We identified the volume of ropivacaine (Naropin) is 1 mL/kg, and the initial concentration is 0.15% based on our pre-experiment and a previous study [6]. We used the sequential allocation scheme designed by Dixon in which the last patient's block outcome was used to determine the next patient's dose [8, 9]. Failure block was defined as intraoperative movement associated with surgical stimulation or increased heart rate or mean arterial pressure of more than 20% of baseline values during surgery. A successful block was defined by completing the operation with stable vital signs. If the previous patient's block was successful, the next patient's concentration was decreased by 0.015%; if the last patient's block is failed, the next patient's concentration was increased by 0.015%. Until 7 crossover points (from failure to success of the block) were produced [7], the study was finished.

All enrolled children fasted from solids for 8 h and liquids for 2 h. Heart rate, respirations, SpO₂ (pulse oxygen saturation), and MAP (non-invasive mean arterial pressure) were monitored continuously after entering the operating room. All patients were placed supine on the operating table

and maintained spontaneous breathing under mask oxygen inhalation 4L/min supply. Each patient was induced with 0.05 mg/kg midazolam, 0.01 mg/kg phencyclidine hydrochloride, 3 mg/kg propofol, and 0.2 µg/kg sufentanil. and anesthesia was maintained with intravenous pumping of propofol at a pumping rate of around 5 mg/kg/min. Meanwhile, we used bis to test the anesthetic effect of this pumping rate and kept intraoperative bispectral index (BIS) values fluctuating between 40–60 and adjusted of propofol pumping rate according to the Bis value. The patient was placed in the lateral position for a caudal block after induction of anesthesia. When induction of anesthesia is complete the child is determined to be breathing steadily. Next, an experienced anesthesiologist performs an ultrasound-guided sacral block. Firstly, the patient was placed in the left lateral position with flexed hips and knees. The skin of the sacrococcygeal regions was fully exposed. The sacral hiatus was located by palpation, and the needle entry point was marked with a marking pen; skin and subcutaneous tissues were sterilized before conducting the caudal block. The position of the sacral lumen was identified using an M-Turbo ultrasound machine (GE venue50; GE, Boston, Massachusetts, USA) at 6–13 Hz (Fig. 1). Then, a 22-gauge needle was advanced close to the sacral lumen by in-plane puncture under ultrasound guidance. The beveled needle tip is to the head; after aspiration of the syringe to ensure no liquor or blood reflux, the prespecified volume of 1 ml/kg ropivacaine was injected into the sacral canal at the same speed (Fig. 2). The operation was started 15 min after the local anesthetic was injected.

The vital signs and SPO₂ were determined within 1, 5, 10, and 15 min after the end of the caudal block. Within 1, 5, 10, 15, 20, 25, 30, 60 min after the operation had started, the end of the process was also included. The procedure is initiated when the patient does not experience a painful reaction while clamping the skin with forceps. When the effect of a sacral block was successful, the child continued to breathe spontaneously and inhaled 4 L/min of pure oxygen through a face mask, anesthesia

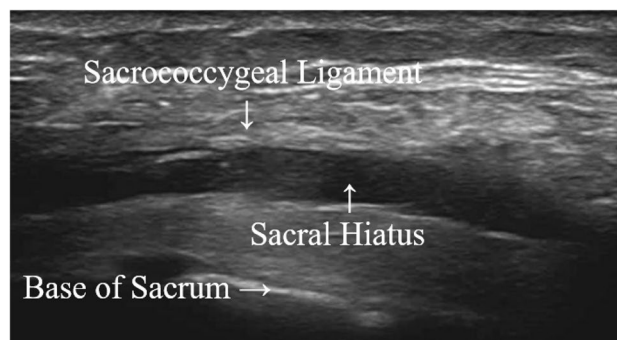


Fig. 1 Cross-sectional ultrasound view of the Sacral

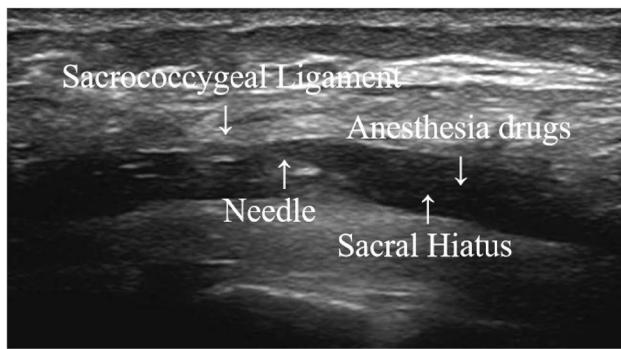


Fig. 2 Ultrasound view of the local anesthetic filled the sacral lumen

was maintained with continuous intravenous pumping of propofol. When the block failed, we performed remedy measures immediately. We administered intravenous injections of Sufentanil and Propofol and placed a suitable laryngeal mask to connect ventilator-assisted ventilation. Follow-up anesthesia was maintained with intravenous pumped propofol and remifentanyl and inhaled sevoflurane. Anesthesia medication is stopped at the end of surgery. After surgery, All the children entered the resuscitation process, and an analgesic pump was routinely used before returning to the ward. when the low concentration of ropivacaine cannot satisfy the surgical analgesia, we will give dezocine 0.1 mg/kg prophylactic analgesia at the end of the surgery before the child wakes up, and then we will give the intravenous analgesic pump (Hydromorphone: pump rate is 3 $\mu\text{g}/\text{kg}/\text{h}$, duration is 48 h) continuous pumping after the child wakes up. When the concentration of ropivacaine was sufficient for surgical analgesia, no prophylactic analgesic medication was given before awakening, and an intravenous analgesic pump (Hydromorphone: pump rate is 3 $\mu\text{g}/\text{kg}/\text{h}$, duration is 48 h) was administered after the child awoke. A routine follow-up was carried out after surgery. Recording the child's general condition throughout anesthesia includes age, gender, weight, operation times, anesthesia time (from the beginning of anesthesia to the termination of anesthetic monitoring, and vital signs were recorded.

In this study, we used Dixon's up-down sequential method. The MEC50 of ropivacaine is calculated as the average of the crossover midpoints using the probit regression method. The MEC95 and the 95% confidence intervals of both concentrations were calculated using Probit regression analysis. General information Data were analyzed by SPSS software, and variables were expressed as the mean \pm SD. The research was performed using the statistical software R for Windows version 4.2.1 and SPSS for Windows version 27.0 (SPSS Inc., Chicago, IL, USA).

Results

49 children undergoing hypospadias repair surgery were assessed for eligibility from March 2022 to November 2022, and three children were identified the needle pierced blood vessels. The recruitment flowchart is shown in Fig. 3. Finally, 22 were in the toddlerhood group and 24 in the preschool group (Figs. 4 and 5). Of the total number of patients, the caudal block was successful in 25 (54%) and failed in 21 (46%). Children's age (months), weight (kg), anesthesia time (min), and operative time (min) are shown in Table 1.

The MEC50 of 1 ml/kg ropivacaine was 0.102% (95% CI 0.099%, 0.138%) in the toddlerhood group and 0.129% (95% CI 0.124%, 0.138%) in the preschool group. The MEC95 of 1 ml/kg ropivacaine was 0.148% (95% CI 0.131%, 0.149%) in the toddlerhood group and 0.162% (95% CI 0.134%, 0.164%) in the preschool group. Our results showed that ropivacaine concentration was statistically different between preschool children and toddlers ($P < 0.001$). Postoperative visits did not reveal any anesthesia-related adverse events.

Discussion

Our study shows that ropivacaine is a safe and effective local anesthetic for caudal block in pediatric patients. In the end, the number of children whose block was judged to be successful was 25, and the number of failures was 21. The reasons for block failure were analyzed as follows. First, the effectiveness of the sacral block is mainly affected by two factors: sacral anesthesia operation technique and the dose of local anesthetic. In this study, technically we used ultrasound to guide the sacral block, which improved the accuracy of the block; so the dose of ropivacaine was the determining factor affecting the success of the block. In this trial, the volume of ropivacaine was 1 ml/kg in all cases, so the effect of sacral block mainly depended on the concentration of ropivacaine, and it can be seen that the lower the concentration of ropivacaine, the higher the number of block failure cases within a certain range. The concentration and volume of local anesthetic largely determine the effectiveness of local anesthesia. In dose-related studies of local anesthetics, ED50 is a good indicator to help clinicians choose appropriate starting doses [10]. For sacral blocks in children, the volume of ropivacaine is usually 1 ml/kg [6]. Hence, in this study, we offer the first estimates of the MEC50 and MEC95 of 1 ml/kg ropivacaine for caudal block in pediatric patients. The MEC50 and MEC95 of 1 ml/

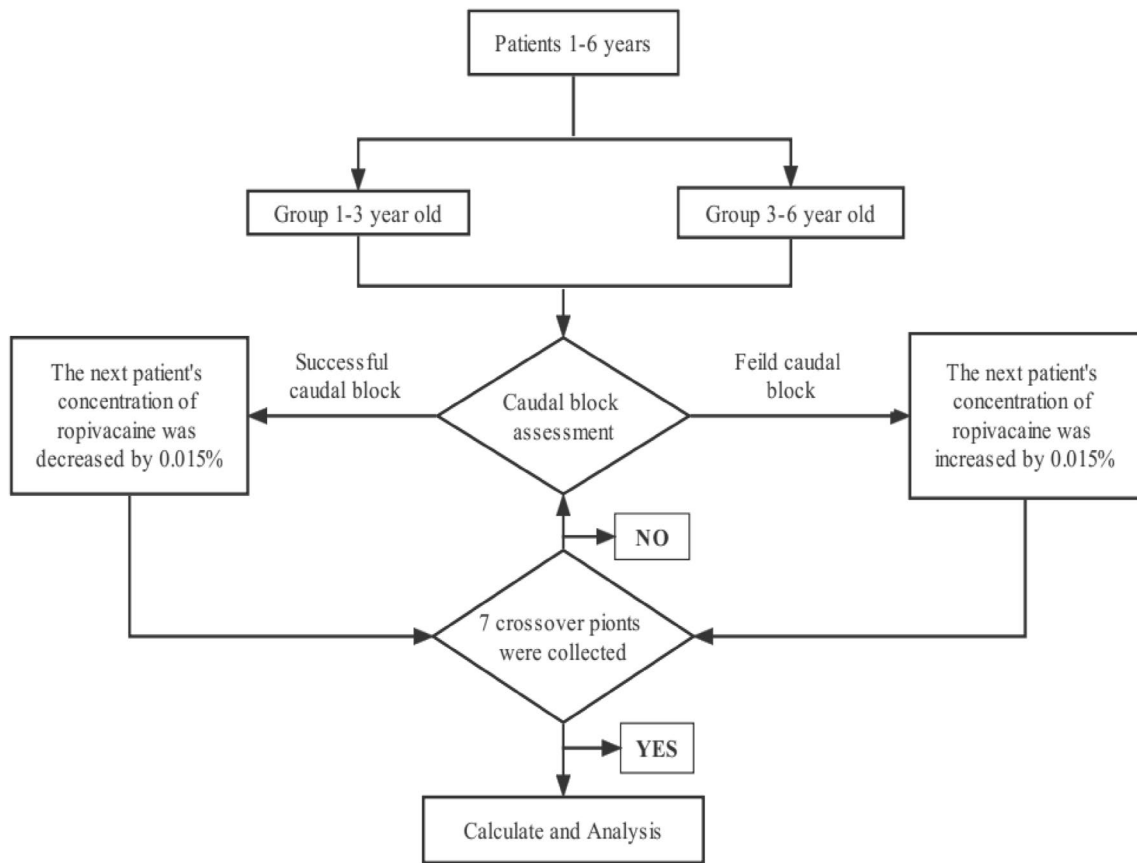


Fig. 3 Participants of the study

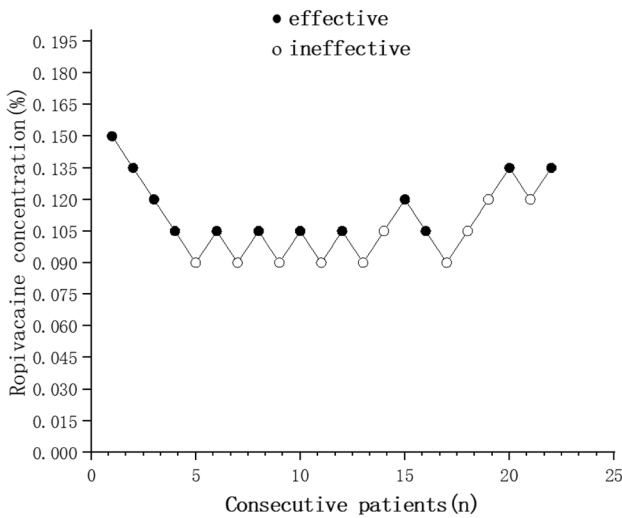


Fig. 4 The concentration of ropivacaine in the toddlerhood group (n = 22)

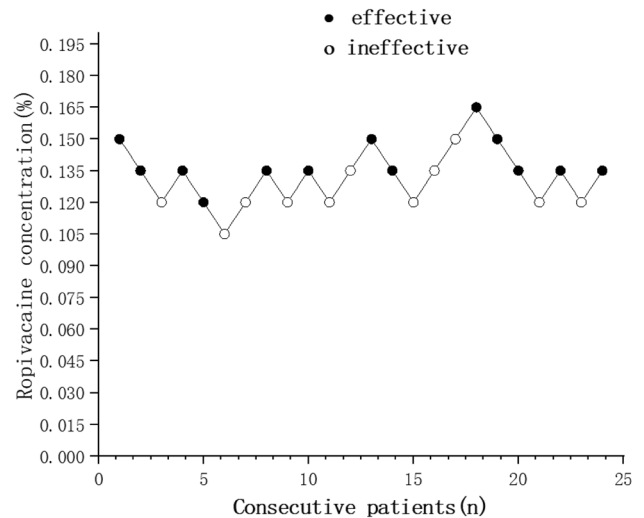


Fig. 5 The concentration of ropivacaine in the preschool group (n = 24)

kg ropivacaine were 0.102% (95% CI 0.099%, 0.138%) and 0.148% (95% CI 0.131%, 0.149%) in the toddlerhood group (1–3 years of age), 0.129% (95% CI 0.124%,

0.138%) and 0.162% (95% CI 0.134%, 0.164%) in the preschool group (3–6 years of age), Our results are close to the current clinical dosing, and this result may guide future

Table 1 General Information of the children

	1–3 years old <i>N</i> =22	3–6 years old <i>N</i> =24
Male <i>n</i> /total <i>N</i> (%)	22/22 (100%)	24/24 (100%)
Age (months), mean (SD)	26.2 (6.03)	52.33 (10.53)
Weight (kg), mean (SD)	11.16 (1.27)	16.29 (2.01)
Anaesthesia time (min), mean (SD)	77.95 (23.42)	79.46(22.81)
Operative time (min), mean (SD)	59.05 (23.25)	59.62(22.87)

Data were presented as means \pm standard deviation (SD) or number (%). Of the total number of patients, the caudal block was successful in 25 (54%) and failed in 21 (46%). No adverse events were observed in either group

clinical dosing. However, we examined only children aged 1–6 years who had hypospadias; the results of our study represent only that population. We studied only the minimum effective concentration of 1 ml/kg ropivacaine, and our results represent only that volume.

Our results showed that ropivacaine concentration was statistically different between preschool children and toddlers ($P < 0.001$). For this finding, we believe that it may be due to differences in neurodevelopment in different age groups, leading to inconsistent doses of ropivacaine in sacral anesthesia. Larger doses of ropivacaine are needed for older children. Age has been shown in previous studies to be an important factor in the effectiveness of local anesthetics [11–13]. Meanwhile, a study reported that “Age emerged as an independent predictor of block failure” [14]. The US Food and Drug Administration (FDA) has advised that repeated or lengthy exposures to anesthetic and sedative drugs before 3 yr of age have the potential to harm the development of children’s brains [19]. Through the above studies and in conjunction with daily clinical use of medications, considering that the development of nervous system morphology and function are different in children of varying age groups, we believe that there may be differences in local anesthetics between these two age groups. Therefore, in this study, we looked into the half-maximal effective concentration of ropivacaine in the toddlerhood group (1–3 years of age) and the preschool group (3–6 years of age) separately. Eventually, our results showed that ropivacaine concentration was statistically different between preschool children and toddlers ($P < 0.001$). This result may be because the diameter of pediatric nerves thickens with age, and the smaller the diameter of the nerve the more likely it is to be blocked.

This study largely reduced intraoperative opioid doses. Sufentanil (0.2 μ g/kg) was injected intravenously at the beginning of anesthesia induction to attenuate the pain upon injection of Propofol and alleviate the pain on the caudal block. However, we think Sufentanil’s residual effect has little impact on skin testing or hemodynamic reaction during surgery. Regional anesthesia and analgesia as adjuncts to decrease opioid use. In the

present study, anesthesia was induced using an opioid dose that was only one-fourth of that used without combined regional blockade. When ropivacaine concentrations approached MEC95, smaller opioid doses were able to meet surgical analgesia needs. Caudal block anesthesia can decrease the need for systemic analgesia, effectively reducing the total dosage of narcotic drugs and muscle relaxants. Using Regional anesthesia while keeping the patient breathing spontaneously can prevent respiratory or hemodynamic compromise and help patients to emerge from anesthesia as fast as possible [15, 16].

In our study, we have determined the 50% minimum effective concentration (MEC50) and the 95% effective concentration (MEC95) of ropivacaine for the caudal block during hypospadias repair surgery of pediatric patients in the toddlerhood group and the preschool group. It has also been previously reported the minimum local anesthetic concentration (MLAC) of ropivacaine for caudal analgesia under general anesthesia with 0.5 MAC enflurane was 0.11% aged 1–5 years [17]. This result lies midway between the two groups of our study (0.102% in the toddlerhood group and 0.129% in the preschool group). In another study, Deng et al. reported that the MLAC of ropivacaine for caudal block under general anesthesia with 0.7 MAC end-tidal sevoflurane was 0.107% in pre-school-age children [18]. In general terms, there were minor differences between our study’s results and those previously published. This may be due to differences in induction drugs as well as intraoperative maintenance anesthesia drugs.

Conclusions

This study showed that children in the preschool group required higher concentrations of ropivacaine than children in the toddler group during ultrasound-guided sacral block combined with non-intubated general anesthesia. At the same time, this method of anesthesia is safe and effective for children undergoing surgery for hypospadias.

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Data availability The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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