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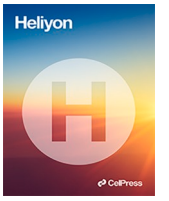

Research article

Effects of single-injection intercostal nerve block as a component of multimodal analgesia for pediatrics undergoing autologous auricular reconstruction: A double-blinded, prospective, and randomized study

Kang Zheng [a], Bin Li [b], Jie Sun [b,*]

[a] Department of Anesthesiology,Nanjing Pukou District Hospital of Chinese Medicine, Nanjing, China
[b] Department of Anesthesiology, Zhongda Hospital, Southeast University, Nanjing, China

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ABSTRACT

Background: : Pain management is essential in postoperative settings, especially with pediatric patients. Donor site pain after rib cartilage harvest is severe, particularly during the early postoperative period. This study aimed to explore the effectiveness of ultrasound guided single-injection intercostal nerve block (ICNB) as a component of multimodal analgesia for pediatrics undergoing autologous auricular reconstruction.

Methods: : Fifty pediatric patients aged 6–16 years and scheduled for 2 rib cartilages harvest surgery were enrolled in this double-blind, prospective and randomized study. Pediatrics were randomly assigned into two groups: the intercostal nerve block group (group B) and the control group (group C). The nerve block was performed with 2 ml 0.25% ropivacaine each intercostal nerve in group B. Patients from group C received Tramadol 2 mg/kg by the end of the surgery as control. Tramadol-based patient-controlled intravenous analgesia and rescue analgesia were given in both groups. The primary outcome was pain scores at early postoperative period (VAS and FLACC scale, 4 h, and 8 h). The secondary outcome was the postoperative Tramadol consumption and time point of first rescue analgesic demand.

Results: : VAS score was significantly lower in group B than group C at 4 h and 8 h postoperatively [2.5(2–5) vs. 4(2.5–5.5), $p = 0.041$ at 4 h; 3(2.5–4.5) vs. 4(3–5), $p = 0.047$ at 8 h]. Total Tramadol consumption in group B decreased significantly in contrast with group C at 8 h ($p < 0.01$), 12 h, 24 h and 48 h ($p < 0.05$, respectively). The first rescue analgesia demand and number of rescue Tramadol in block group was considerably delayed or reduced than control group ($p < 0.01$, $p < 0.05$, respectively).

Conclusions: : Our findings indicated that ultrasound guided ICNB slightly but significantly reduced pain scores, and Tramadol consumption in pediatric patients after rib cartilage harvest as compared to who didn't receive nerve block at 4 h and 8 h postoperatively. Unified ICNB ropivacaine dosage might detrimental to providing superior analgesia.

* Corresponding author. Department of Anesthesiology, Zhongda Hospital, Southeast University School of Medicine, 87 Dingjiaqiao, Nanjing, China.
E-mail address: dgsunjie@hotmail.com (J. Sun).

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1. Introduction

Microtia, as a congenital malformation of auris externa, is reported to occur up to 0.83 to 4.34 per 10,000 births, with higher incidences among males and those of Hispanic and East Asian heritage [1]. Rib cartilage-based autologous auricular reconstruction is the classic and most widely performed technique for microtia patients, rib cartilage harvest acts as one of the vital procedures of reconstruction surgery. The rib cartilages become tough and thick enough for auricula sculpture from 6 to 10 years old. Therefore, the majority of surgical patients are children. Postoperative analgesia in pediatric patients is intractable due to characteristics of pharmacotherapy in children and the postoperative pain from both the donor site and ear area.

After autologous auricular reconstruction, relieving pain from two independent surgical sites is the central task of postoperative pain management. Tramadol based-patient-controlled intravenous analgesia (PCIA) has been used for many years in our center, pain in the ear area is nicely covered by PCIA, yet the donor site pain is not. For this reason, we aimed to find an effective way to relieve the postoperative donor site pain, especially during the early postoperative period.

Intercostal nerve block (ICNB) has been used as an adequate postoperative analgesia after thoracic or upper abdominal surgery, including rib cartilage harvest surgery, in adult patients for several decades [2–4]. However, reports on children are very limited [5]. To the best of our knowledge, there is no previously published double-blind, prospective, and randomized study of ultrasound (US)-guided single-injection ICNB as part of multimodal analgesia for postoperative analgesia with rib cartilage harvest pediatrics.

In this study, we hypothesized that compared to Tramadol-based postoperative analgesia, US-guided single-injection ICNB plus PCIA, might provide superior analgesic effect in pediatric rib cartilage harvest patients during the early postoperative period. The primary outcome of our study was pain scores at early postoperative period [VAS (Visual Analogue Scale) and FLACC (Face, Legs, Activity, Cry, Consolability scale) scale, 4 h, and 8 h]. The secondary outcome measure was postoperative analgesic consumption and time point of first rescue analgesic demand.

2. Methods

The present trial was conducted in compliance with the International Conference on Harmonization - Good Clinical Practice guidelines and Declaration of Helsinki [6,7]. This double-blind, prospective, and randomized trial was approved by Zhongda Hospital Ethical Committee (2015ZDSYLLO51.0) and prospectively registered at Chinese Clinical Trial Registry (ChiCTR-INR-15007469).

Patients were eligible for this trial based on the following criteria: aged between 6 and 16 years (inclusive), American Society of Anesthesiologists (ASA) physical status I, planned to harvest 2 rib cartilages, fluent in Mandarin, able to correctly recognize and express the degree of pain and willing to employ PCIA. Exclusion criteria included history of allergy to any of the anesthesia drugs which included in the trial, coagulation dysfunction, local skin infection, history of chronic opioid use or thoracic surgery, receiving any analgesic within 48 h before surgery, whom could not correctly use the pain scales, and patients who have already recruited in other clinical trials.

Written informed consent was obtained from parent or legal guardian of pediatric patients on the night before surgery, children were familiarized and educated with PCIA and pain score assessment. Phenobarbital 2 mg/kg was given as premedication via intramuscular injection before surgery. Since patients were transferred to the operating room, standard monitoring devices such as pulse oximeter, noninvasive blood pressure, electrocardiograph, and capnography were performed. General anesthesia induction was performed by infusing midazolam 0.06 mg/kg, propofol 2–4 mg/kg, fentanyl 2 μg/kg, and cisatracurium 0.1 mg/kg to facilitate tracheal intubation. Propofol, remifentanil, sevoflurane and cisatracurium were employed for anesthesia maintenance. All patients received ondansetron 0.1 mg/kg for preventing postoperative nausea and vomiting (PONV).

Pediatric patients were randomly assigned into either the ICNB group (group B) or control group (group C) in a 1:1 ratio. Randomization was performed with sequentially numbered opaque sealed envelope technique by an independent staff [8]. Both observer and patients were blinded to the group assignment and interventions. By the end of the surgery, a specialized anesthetist performed all ICNB 2ml/rib 0.25% ropivacaine (group B) or Tramadol injection 2 mg/kg iv (group C).

US-guided single-injection ICNB was performed under general anesthesia with in-plane approach in all patients at the end of the

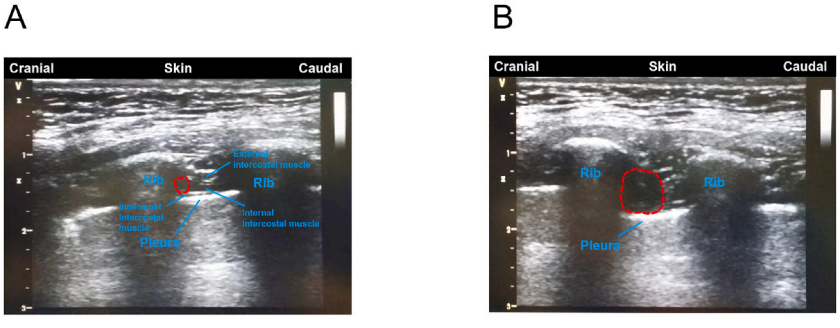

Fig. 1. Ultrasound scans of the intercostal nerve area before and after ICNB.
Legend: A, before ICNB, intercostal nerve and surrounding structures were identified. B, after ICNB, intercostal nerve was surrounded by LA.

surgery. Briefly, patients were kept in a supine position, skin disinfection with povidone-iodine. Firstly, particular operated ribs, pleura, and intercostal muscles were identified before puncture at the midaxillary line, the location of the intercostal nerve was identified with the red circle in Fig. 1A. Then, placed the needle into the space between internal intercostal muscle and innermost muscle. Afterward, aspirating the syringe to ensure it is not in a blood vessel. By the end, all patients from group B received 2ml/rib of 0.25% ropivacaine for 2 ribs as nerve blocking. After the blockage, local anesthetic (LA) surrounded the intercostal nerve in the red circle as shown in Fig. 1B. The dosage of ropivacaine is much less than the maximum recommended dose for each patient.

All patients were transferred to the post-anesthesia care unit (PACU), tracheal extubation was performed in PACU under the supervision of one experienced anesthesiologist. The VAS score was less than 4 before leaving PACU. Patients in both groups received PCIA. The following PCIA formula was used: saline 100 ml with 10 mg/kg Tramadol and 0.2 mg/kg of ondansetron, a background dose of 2 ml/h, a single bolus dose of 2 ml with 15min bolus locking time. If 2 continuous blouses of PCIA did not relieve pain satisfyingly, Tramadol 2 mg/kg was given as rescue analgesia. Celecoxib oral suspension 3 mg/kg were given twice a day in ward.

A, before ICNB, intercostal nerve and surrounding structures were identified. B, after ICNB, intercostal nerve was surrounded by LA. ICNB, Intercostal Nerve Block; LA, local anesthetic.

The anesthesia time, intraoperative propofol, and intraoperative analgesic consumption (morphine equivalents of fentanyl and remifentanil [9]) were recorded. The surgical variables were also recorded.

2.1. Outcome measures

The primary outcome was pain scores at the early postoperative period (4 h, 8 h). Including VAS assessed by children and FLACC assessed by parents or legal guardians. The VAS consists of a 10 cm line segment, the 2 ends representing 0 (no pain) and 10 (pain as bad as it could possibly be). Patients were asked to mark their current pain level on the line. The FLACC is a 0–10 scores system which incorporates five categories of pain behaviors. The FLACC score represents pain level of pediatrics in the perspective of parents or legal guardians. Secondary outcomes were to compare postoperative Tramadol consumption, time point of the first rescue analgesia, and number of rescue analgesia. We recorded VAS before pediatric left PACU. Incidence rate of PONV, SpO_2, respiratory-related complication (e.g., dyspnea, hypoxemia), pleura-related complication (e.g., pleura injury, pneumothorax) and local anesthetic systemic toxicity were recorded. A pain management specialist nurse who was blinded to the trial was responsible for the postoperative follow-up.

2.2. Statistical analysis

The sample size was determined from previous ICNB studies after thoracic surgery [10] and our pilot study. We recruited 5 patients

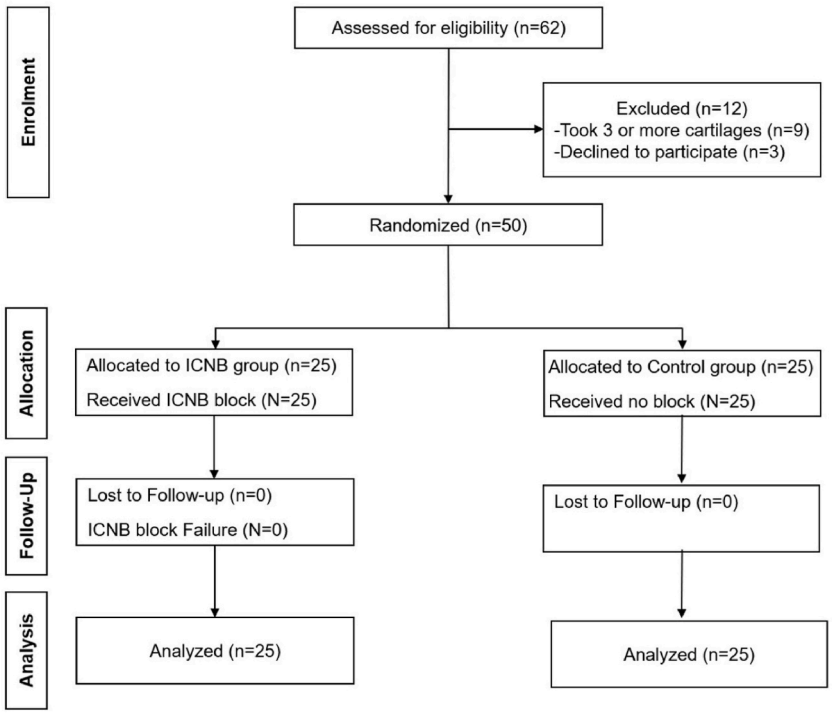

Fig. 2. Flow diagram of CONSORT.
Legend: ICNB, Intercostal Nerve Block.

in each group in our pilot study, which showed that VAS at 4 h postoperative was 3.7 ± 1.5 in the control group and 2.1 ± 1.6 in the block group. We assuming an α error = 0.05 with a power of 0.90, the calculation with G*Power programmer (v3.1, University Kiel, Germany) resulted that at least 21 patients were required per group. Considering possible drop-outs, we decided to include 25 pediatrics in each group.

All statistical analyses were performed by GraphPad Prism version 9.2.0 for Windows (GraphPad Software, San Diego, California USA). Kolmogorov-Smirnov test was employed for normality of data distribution analysis. Quantitative data were expressed in the form of mean ± standard deviation or medians (interquartile ranges). Categorical variables and counts were presented as numbers (percentage). Continuous variables, demographic data, and Tramadol consumption were analyzed by Student's t-test or Mann Whitney test depending on whether the data were distributed normally or not. VAS and FLACC scores were analyzed by Repeated Measures ANOVA. Pearson's Chi-square test was performed for the comparison of categorical variables, e.g., the incidence of postoperative nausea and vomit. We used a univariable Cox proportional hazards model to compare the time of the first rescue medication. $p < 0.05$ was considered statistically significant.

3. Results

Sixty-two pediatric patients were enrolled in this trial. 12 patients were excluded, 9 of them were excluded since more than 2 rib cartilages were harvested, 3 pediatrics declined to receive rescue analgesic. Therefore, 25 patients were randomly assigned to the ICNB group and 25 to the control group. No patient was lost to follow-up. All 50 pediatric patients finished the trial and were included in the outcome analysis. Consolidated Standards of Reporting Trials (CONSORT) flow diagram was applied for patient enrolment and allocation (Fig. 2).

As shown in Table 1, the demographic characteristics, includes age, gender distribution, height, weight, and BMI, of two groups were comparable). Regarding to intraoperative and surgical variables, no between-group difference was observed in terms of duration of anesthesia or surgery, intraoperative anesthetic consumption and surgical site.

Single-injection ICNB significantly reduced pain scores at the early postoperative phase. As shown in Table 2, pain was well controlled when patients leaving PACU at 0 h, mean VAS scores at 4 h and 8 h were significantly reduced in group B than that in group C ($p = 0.041$ at 4 h, $p = 0.047$ at 8 h), respectively. FLACC also showed a considerably lower score at 4 h ($p = 0.048$) in the ICNB group, compared with the control group.

As shown in Fig. 3A, total Tramadol consumption in group B was significantly less than those in group C at 8 h, 12 h, 24 h and 48 h (Fig. 3A). Regarding rescue analgesic, notably less rescue Tramadol was expended in group B than group C during 48 h after surgery (Fig. 3B). Meanwhile, Tramadol consumption from PCIA was similar in two groups. The first rescue analgesic demand also exhibited a statistical postpone in group B than in group C [HR = 0.34, 95% CI (0.18–0.64), Log-rank $p < 0.001$; Fig. 4A], around 3 h (Fig. 4B). Meanwhile, patients in group B received significantly less doses of rescue analgesia than patients in group C (Fig. 4C).

No statistical difference of postoperative SpO_2 level was found between ICNB and control group. No respiratory-related complications, e.g. dyspnea or hypoxemia was observed in both groups. No pleura injury, pneumothorax was found in two groups. No syndromes of LA intoxication were found in group B. The incidence of PONV was similar in both groups. In group B, there were 11 patients had nausea after surgery, and 3 of them experienced vomiting. In group C, 4 patients vomited, and 13 patients had nausea. There was no statistically significant difference between the two groups regarding postoperative nausea ($p = 0.286$) or vomiting ($p = 0.957$).

4. Discussion

Our findings indicated that ultrasound guided single-injection ICNB slightly but significantly reduced pain score in pediatrics after rib cartilage harvest during the early postoperative period (4 h and 8 h), compared with the control group. Total Tramadol consumption was also significantly decreased in group B. Regarding rescue analgesia, consumption of rescue Tramadol, number of rescues

Table 1
Baseline data.

	ICNB group (n = 25)	Control group (n = 25)
Demographic data		
Age,media (IQR) (year)	9.4 (6–11)	9.6 (6–12)
Gender Female, %	52%	48%
Weight (kg)	33.1 ± 10.1	32.2 ± 9.3
Height (cm)	136.4 ± 11.8	133.8 ± 13.5
BMI (kg/m2)	17.6 ± 4.0	17.8 ± 3.0
Intraoperative variables		
Duration of anesthesia (min)	317.2 ± 41.2	305.0 ± 49.1
Intraoperative analgesic consumption (morphine equivalents, mg)	260.2 ± 92.4	244.7 ± 85.1
Propofol (mg)	769.7 ± 106.1	740.0 ± 114.5
Surgical variables		
Duration of surgery (min)	281.4 ± 43.6	270.2 ± 46.8
Operation side (Left/Right)	9/16 (36%)	11/14(44%)

ICNB, Intercostal Nerve Block; IQR, Interquartile range; BMI, Body Mass Index.

Table 2
Postoperative VAS scores and FLACC scores.

	ICNB group (n = 25)	Control group (n = 25)	*P* value
VAS scores			
0 h	1.5 (1–3)	2 (1–3)	0.993
4 h	2.5 (2–5)	4 (2.5–5.5)	**0.041**
8 h	3 (2.5–4.5)	4 (3–5)	**0.047**
12 h	3 (2–6)	3 (2–6)	0.748
24 h	2 (1–4)	2 (1–4)	>0.999
48 h	1 (1–2)	1 (1–2)	>0.999
FLACC score			
4 h	2.5 (2–5)	3.5 (2–6)	**0.048**
8 h	3 (2–5)	3(2–5)	0.683
12 h	3 (1–4.5)	3 (1–4.5)	0.119
24 h	2 (1–3)	2 (1–4)	0.995
48 h	1 (0.5–1)	1 (0–1)	0.989

P value < 0.05 were in bold. FLACC, Face, Legs, Activity, Cry, Consolability scale; ICNB, Intercostal Nerve Block; VAS, Visual Analogue Scale.

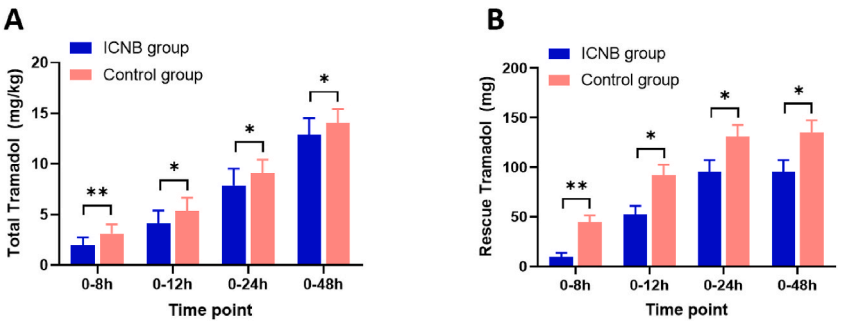

Fig. 3. Total and rescue Tramadol consumption after rib cartilage harvest surgery.
Legend: A, total postoperative Tramadol consumption. B, Postoperative rescue Tramadol consumption. ICNB, Intercostal Nerve Block. *p < 0.05, **p < 0.01.

analgesia, and first rescue analgesic demand were significantly reduced or delayed in the ICNB group than the control group. To the extent of our knowledge, this study is the first double-blind, prospective, and randomized trial that demonstrated the efficiency of US-guided single-injection ICNB-based multimodal analgesia after rib cartilage harvest in pediatric patients.

Our results revealed that during the early postoperative phase, ICNB-based multimodal analgesia provides slight but significant improved pain-relieving than intravenous opioids. Donor site pain is the most common complaint after rib cartilage harvest [11]. Compared with other thoracic surgeries, pain after rib cartilage harvest is more severe and more centralized on the particular cartilage donor site area. Our data revealed that ICNB provided a potent analgesic effect on the chest surgical region. This finding is consistent with previous studies with pediatric patients after rib fracture, thoracotomy and other thoracic surgeries [12,13]. The pain score reduction in this study is statistically significant but marginal, that may due to the unified LA dosage in all patients. The dosage of 2ml/rib Ropivacaine may sufficient for young low BW patients, but not enough for the higher BW ones. That may resulted in uneven pain relieving in ICNB group patients, then affected the pain score reduction.

Postoperative analgesic consumption was significantly reduced after receiving single-injection ICNB. Several reports revealed that ICNB could reduce postoperative analgesic consumption after types of thoracic surgeries [3,14–16]. Rice and colleagues found that 24 h postoperative analgesic consumption was reduced in adult patients received ICNB than whom received epidural anesthesia [17]. Our study showed that 48 h total Tramadol consumption decreased significantly after surgery in ICNB group than control group, which is consistent with previous studies. In the present trial, the reduction of Tramadol consumption might mainly due to less usage of rescue analgesia Tramadol (Fig. 3 B), since the Tramadol consumption from PCIA were similar in two group. Both delayed first rescue analgesia demand and reduced rescue analgesia doses contributed to reducing rescue Tramadol consumption.

Multimodal analgesia has been shown to provide improved analgesia and better patient satisfaction than opiate-based analgesia [18,19]. Nerve block is a pivotal component of multimodal, it offers profound pain relief, ensures a more rapid recovery with fewer opioid-induced side effects [18]. In the present trial, both Tramadol-based PCIA and ICNB are vital in relieving postoperative pain. As pediatric patients suffered pain from both donor site and ear area, intravenous Tramadol provides a systematic and stable analgesia effect, which reduces the pain from both regions [20]. ICNB enforced the analgesic effect of PCIA in the area of rib cartilage harvest and saved postoperative analgesic.

The side effects associated with ICNB, such as pneumothorax, local anesthesia systemic toxicity, or hypoxemia, did not occur in the present study. This might be due to the use of the US-guided blocking technique. Several studies have provided evidence on the safety

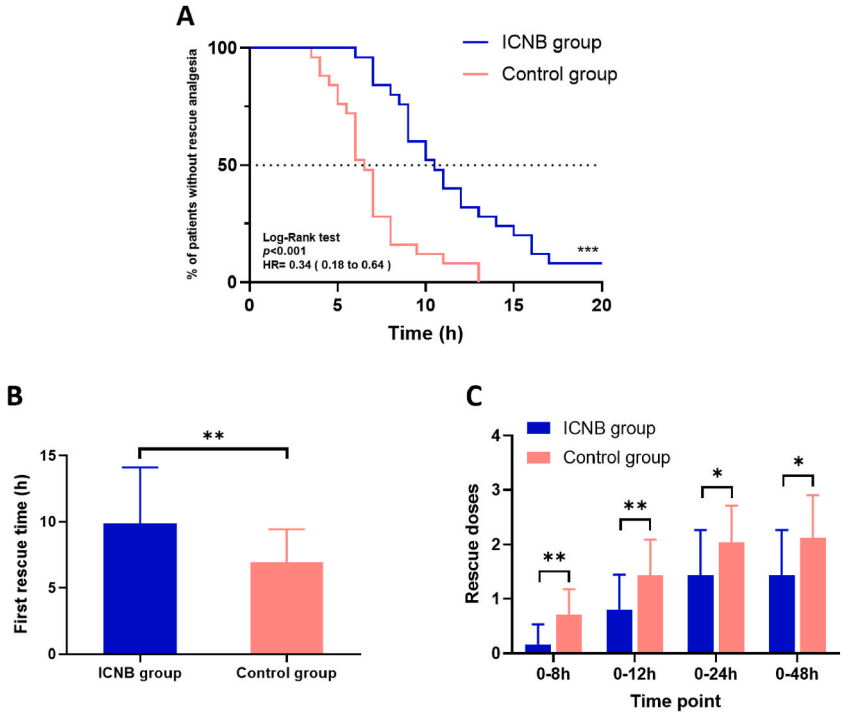

Fig. 4. The time point and number of rescue analgesic demand.
Legend: A, time point of first rescue analgesic injection. B, average time of first rescue analgesic demand. C, number of rescue analgesic injections. ICNB, Intercostal Nerve Block. *p < 0.05, **p < 0.01.

of a single injection of ICNB [21]. US provides high-quality real-time view of the certain nerve and surrounding tissues, enable the block needle placed more accurate without intravascular injection. Munirama et al. found that an almost eight-fold reduction in intravascular injection by using US guided nerve block technique [22]. Meanwhile, the procedure of US-guided ICNB only takes fairly short time, we found duration of surgery and anesthesia in ICNB group is comparable to control group. This trial demonstrated that US-guided single-injection ICNB is a safe and time-efficiency method for preventing donor-site pain in children after rib cartilage harvest. This finding may only apply to US-guided ICNB.

In the context of multimodal analgesia, single-injection ICNB would probably be the most appropriate postoperative analgesic technique for pediatrics received rib cartilage harvest. Researchers reported that ICNB provides comparable analgesia to epidural anesthesia, which is believed the gold standard analgesia, and induced fewer adverse effects in adults and pediatrics after thoracic surgery [17,23]. Moreover, epidural anesthesia in children often takes a longer learning curve and may induce more complications than ICNB [24]. Centralized severe pain in the rib cartilage area is the feature of donor site pain [25]. ICNB provides potent, centralized analgesia along the certain ribs. Furthermore, previous studies showed that ICNB consumes much less LA to obtain comparable analgesia as contrast to paravertebral block and continuous wound infiltration after thoracic surgery, especially in the first 8–12 h [3, 26].

This trial has numbers of limitations. Firstly, the age range of pediatrics is wide (6–16 years), its better to classify age range in narrow intervals (e.g. 1–3, 3–6, 6–12 or 12–18 years) since each interval have its physiologic and anatomic characters. Secondly, we only included 2 rib cartilages harvest pediatrics. The safety and efficiency of single injection ICNB in patients who harvested 3 or more cartilages are required to be testified. Thirdly, we gave same dosage of LA to all patients in group B. As heterogeneity of height and bodyweight is large among children in this trial, individualized medicine strategy should be performed in clinic practice and study in the future.

5. Conclusions

In summary, donor site pain is one of the common complaints after rib cartilage harvest surgery in pediatrics. US-guided ICNB slightly but significantly reduced pain scores, Tramadol consumption in those patients as compared to who didn't receive nerve block at 4 h and 8 h postoperatively. Unified ICNB LA dosage might detrimental to providing superior analgesia.

Declarations

Ethics approval and consent to participate

This trial was approved by the ethics committee of the Zhongda Hospital, Southeast University (2015ZDSYLLO51.0) and written informed consent was obtained from parent or legal guardian of pediatric patients. All methods in this trial were carried out in accordance with relevant guidelines and regulations. This trial was registered on the platform of Chinese Clinical Trial Registry on 27/11/2015 (Registration number: ChiCTR-INR-15007469).

Consent for publication

Not applicable.

Author contribution statement

Kang Zheng: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper. Bin Li: Contributed reagents, materials, analysis tools or data. Jie Sun: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

The datasets generated and/or analyzed during the current study are not publicly available due to the local regulations but are available from the corresponding author on reasonable request.

Declaration of competing interest

The authors declare no competing interests.

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List of abbreviations

ICNB	Intercostal nerve block
ASA	American Society of Anesthesiologists
PCIA	Patient-controlled intravenous analgesia
US-guided	Ultrasound-guided
LA	Local anesthetic
PACU	Post-anesthesia care unit
VAS	Visual Analogue Scale
FLACC	Children and Face, Legs, Activity, Cry, Consolability scale
PONV	Postoperative nausea and vomiting
CONSORT	Consolidated Standards of Reporting Trials
MI	Body mass index

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