Heart Surgery Forum 2023; 26(5): E519–E524
doi: 10.59958/hsf.6721

Article

Assessment of Total Ropivacaine Concentration in Blood after Bilateral Pecto-Intercostal Fascial Block Combined with Rectus Sheath Block in Cardiac Surgery Patients

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Submitted: 14 August 2023 Revised: 16 September 2023 Accepted: 26 September 2023 Published: 17 October 2023

Abstract

Objectives: Pecto-intercostal fascial block (PIFB) and rectus sheath block (RSB) have been combined to offer better analgesia for cardiac surgery patients, but safety of the analgesic protocol with a large volume of ropivacaine is uncertain. **Methods**: This is a prospective observational study at Peking University People's Hospital to investigate the pharmacokinetic profile of ropivacaine after combined regional blocks. Patients undergoing elective cardiac surgery by a median sternotomy were enrolled to receive bilateral PIFB and RSB with 70 mL 0.3% ropivacaine (total dose 210 mg). Blood was sampled at 5, 10, 15, 30, 60, 90 and 120 mins after blocks. Total blood concentration of ropivacaine for patients were measured. **Results**: Ten patients were enrolled and analyzed. The peak total ropivacaine concentration varied from 0.67 to 2.42 μg/mL. Time to reach the peak values mainly located between 10 and 30 mins after the performance. No patients had ropivacaine concentration values above toxic threshold (4.3 μg/mL), and there were no systemic toxicity symptoms during the perioperative period. **Conclusions**: PIFB combined with RSB in a general injection of 70 mL 0.3% ropivacaine does not give rise to toxic levels, and it is an effective and safe analgesic protocol for cardiac surgery patients.

Keywords

pecto-intercostal fascial block; ropivacaine; rectus sheath block; cardiac

Introduction

Pain after cardiac procedures is catastrophic and persistent, and many patients endure more pain postoperatively than they expect to preoperatively [1]. Adequate analgesia is essential to enhance recovery. In recent years, fascial plane blocks have become available in cardiac surgery as part of multimodal analgesia. Considering the multidimensional pain in cardiac surgery, pecto-intercostal fascial block (PIFB) and rectus sheath block (RSB) have been combined to cover the pain generated from incision of sternotomy and subxiphoid chest tube [2,3].

The potency, concentration and volume of local anesthetics used in regional techniques have been discussed to achieve a balance between efficacy and safety. For facial plane blocks, known as "volume blocks", analgesia depends on the sufficient spread of local anesthesia with adequate volume [4]. The larger the volume of a single injection, the wider the contact area with adjacent tissues, and the more local anesthetics would be absorbed into the blood. The product of concentration and volume is the real dose for a single fascial plane injection of local anesthetics. The maximum allowed milligram dose of local anesthetics may vary for patients with cardiovascular diseases compared to healthy volunteers, as changing cardiomyocyte intracellular calcium dynamics would mediate local anesthetic cardiac toxicity [5]. Besides, the absorption of local anesthetics may be attenuated due to insufficient tissue perfusion resulting from decreased cardiac function. The changes in the plasma concentrations of local anesthetics with larger volumes after a single injection into the fascial planes for patients undergoing cardiac surgery are still uncertain.

This observational study is intended to estimate peak total ropivacaine concentrations in plasma after ultrasound-guided PIFB combined with RSB by a relatively high volume of ropivacaine (70 mL, 0.3%) and evaluate the safety of this analgesic pattern for cardiac patients.

Methods and Materials

Patients

This research was approved by Ethical Review Committee of Peking University People's Hospital (#2022PHB179-001). Patients aged 18 to 75 years who

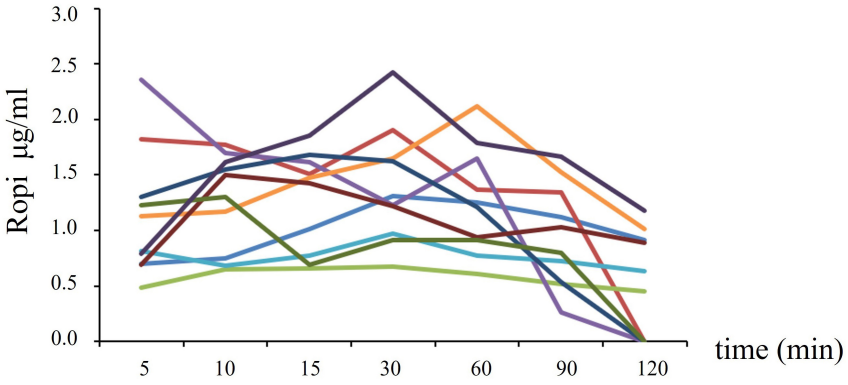

Fig. 1. Total ropivacaine concentration versus time profile for all patients.

were judged as American Society of Anesthesiologists II~III and scheduled for PIFB and RSB before elective cardiac surgery by a median sternotomy were included. Patients with known allergy to ropivacaine, coagulation disorders, infections at puncture sites, opioid abuse and cognitive dysfunction were excluded. Written informed consent was obtained from all the patients.

Anesthesia and Analgesia

All patients were continuously monitored by noninvasive arterial blood pressure, five-lead electrocardiography (ECG), pulse oxyhemoglobin saturation, invasive arterial blood pressure, temperature, urine output and bispectral index (BIS). Anesthesia induction was performed with 0.02–0.04 mg/kg midazolam, 0.2–0.4 mg/kg etomidate, 1–1.5 μg/kg sufentanil and 0.2–0.3 mg/kg cisatracurium. Anesthesia maintenance was performed with propofol, sevoflurane, dexmedetomidine and cisatracurium to guarantee the BIS of approximately 45–55. Bolus sufentanil (0.3–0.5 μg/kg) and vasoactive drugs were given by supervising anesthesiologists. After surgery, patients were transferred to the intensive care unit (ICU) for extubation and further medical care. All patients received patient-controlled intravenous analgesia (PCIA) with a standard regimen of hydromorphone (no basal infusion, 0.2 mg bolus and 10-minute lockout intervals). Postoperative pain was assessed using a 10-point numeric rating scale (NRS) at rest or deep breath at 12, 24 and 48 hours after surgery.

Combined Regional Block Performances

Bilateral PIFB was performed at supine position under ultrasound guidance after anesthesia induction. The high-frequency linear ultrasound probe (EPIQ7C, PHILIPS, Amsterdam, The Netherlands) was placed 2–3 cm at the fourth intercostal space next to the sternum. A 21-gauge needle (SonoPlex STIM, PAJUNK, Geisingen, Germany) was inserted into the plane between the pectoralis major muscle and intercostal muscle using an in-plane technique. After verification by visualizing the muscle separation upon injection of saline, 20 mL 0.3% ropivacaine containing 2.5 mg dexamethasone was delivered to each side.

Bilateral RSB was performed after PIFB with the same position and probe. The probe was placed next to the xiphoid in the epigastric region. The needle was inserted into the plane between the rectus abdominal muscle and its posterior sheath. After verification by visualizing the structure separation upon injection of saline, 15 mL 0.3% ropivacaine containing 2.5 mg dexamethasone was delivered to each side.

Blood Samples

Blood samples were obtained at 5, 10, 15, 30, 60, 90 and 120 mins after PIFB and RSB procedures from the radial arterial cannula. Subsequent blood samples were waived when cardiopulmonary bypass started. Plasma samples were reserved frozen at –80 °C for 2–4 months prior to analysis. An ultra-high performance liquid chromatography-tandem triple quadrupole mass spectrometry method was established to determine total ropivacaine concentrations in plasma at different timepoints. The definite and validation characteristics of this method have been introduced [6].

Statistics

All statistical analyses were performed using GraphPad Prism 9.0 software (GraphPad Prism, San Diego, CA, USA) for Windows. The results are presented as mean (standard deviation).

Results

Ten patients were enrolled and analyzed. Demographic characteristics, peak total arterial ropivacaine concentration (Cmax) and time to reach Cmax (Tmax) are shown in Table 1. The specific ropivacaine concentration at different timepoints for all patients are shown in Fig. 1. The peak total ropivacaine concentration varied from 0.67

Table 1. Demography characteristics and peak ropivacaine concentration (μg/mL).

Patient	Age (y)	Gender	Weight (kg)	EF before surgery	ASA	Surgery	CPB	Surgical time (min)	Anesthetic time (min)	Ropivacaine		
										Dose (mg/kg)	Cmax (μg/mL)	Tmax (min)
1	66	Male	76	65	III	CABG	No	319	405	2.8	1.31	30
2	57	Male	68	65	III	AVR	Yes	400	497	3.1	1.90	30
3	73	Female	63	63	III	CABG	No	261	342	3.3	0.67	30
4	58	Female	70	67	III	MVR	Yes	327	430	3.0	2.36	5
5	70	Female	75	53	III	CABG	No	373	480	2.8	0.97	30
6	65	Male	70	58	III	CABG	No	246	320	3.0	2.12	60
7	51	Male	53	56	III	MVR	Yes	394	510	4.0	1.68	15
8	60	Male	81	64	III	CABG	No	317	405	2.6	1.50	10
9	47	Female	60	68	III	AVR	Yes	346	452	3.5	1.30	10
10	66	Female	61	58	III	CABG	No	278	372	3.4	2.42	30

ASA, American Society of Anesthesiologists; AVR, aortic valve replacement; CABG, cardiac artery bypass graft; CPB, cardiopulmonary bypass; EF, ejection fraction; MVR, mitral valve replacement.

Table 2. Postoperative NRS and clinical outcomes.

Patient	NRS (R/D) at 12 h	NRS (R/D) at 24 h	NRS (R/D) at 48 h	Hydromorphone consumption within 24 h (mg)	Hydromorphone consumption within 48 h (mg)	Pain at the chest tube within 48 h	Time to extubation (h)	LOS in ICU (h)	Time to chest tube removal (h)	LOS in hospital (d)
1	0/1	0/2	0/1	3.0	5.4	No	4.0	21.0	70.0	13
2	1/4	1/2	0/2	4.0	5.0	No	4.5	21.8	69.0	11
3	-	2/2	2/2	2.2	5.0	No	16.0	44.5	72.0	10
4	1/1	1/1	0/0	2.4	3.6	No	8.2	20.7	74.0	10
5	0/0	0/1	0/0	1.6	5.0	No	9.3	44.0	75.0	19
6	0/2	0/2	0/1	3.4	6.0	Yes	8.8	45.5	73.5	12
7	4/5	0/2	0/1	1.8	3.6	No	10.3	51.0	69.0	15
8	3/4	2/3	1/2	3.6	4.4	Yes	10.5	40.3	66.3	8
9	-	0/1	0/1	2.2	2.2	No	16.0	49.5	70.0	9
10	0/1	0/1	0/1	0.6	3.4	No	7.0	46.4	71.7	11

ICU, intensive care unit; LOS, length of stay; NRS (R/D), numeric rating scale at rest and deep breath.

to 2.42 μg/mL in our research. The ropivacaine concentration did not exceed 4.3 μg/mL, and there were no systemic toxicity symptoms through the monitoring of BIS and ECG (abnormal brain electrical waves and malignant arrhythmia) during the perioperative period. Postoperative NRS at rest and deep breath within 48 hours and other recovery outcomes are presented in Table 2. Two patients complained of pain at the drainage site, and three patients endured moderate to severe pain within 48 hours.

Discussion

Our research proved that PIFB combined with RSB, a total injection of 70 mL 0.3% ropivacaine, is safe in cardiac surgery. The peak total arterial ropivacaine concentration varied from 0.67 to 2.42 μg/mL and no systemic toxicity symptoms arose during the perioperative period.

Ropivacaine is a long-acting local anesthetic belonging to amide group and has been widely used in clinical situations due to its sensorimotor differentiation blockage and enhanced safety [7]. Actually, all local anesthetics present certain toxicity, and the toxicity correlates with their lipophilicity [8]. Ropivacaine may possess less cardiovascular and central nervous system toxicity than bupivacaine. However, both bupivacaine and ropivacaine inhibit SCN5A-encoded cardiac Na^+ channel in the same mode of action, and the modest variations in cardiotoxicity between two drugs are associated with dosages used in clinical settings [9]. In addition, in the isolated rat heart, lipid emulsion improves recovery from bupivacaine rather than ropivacaine induced cardiac arrest [10]. Therefore, we must remain cautious about ropivacaine-induced systemic toxicity, especially when a large volume of ropivacaine is applied in patients undergoing cardiac procedures.

This study confirms that PIFB combined with RSB is safe in cardiac surgery, and the peak total arterial ropivacaine concentration varied from 0.67 to 2.42 μg/mL. It has been reported that the mean plasma concentration of ropivacaine for neurological symptoms after intravenous infusion of ropivacaine in healthy volunteers is 4.3 and 2.2 μg/mL (arterial and venous) [11]. Whether nervous and cardiac symptoms would emerge at the same time are uncertain when ropivacaine is absorbed from tissues rather than intravenously injected, as central nervous system stimulation produces initial cardiovascular activation. However, in this study, the ropivacaine concentration did not exceed 4.3 μg/mL, and there were no nervous or cardiac toxicity symptoms in any patients from the perspective of BIS and ECG.

No adverse events occurred when ropivacaine plasma concentration remained below toxic concentrations [12], and such a finding is not surprising. Torup and colleagues performed bilateral transversus abdominis plane blocks with 40 mL 0.5% ropivacaine, and one-third of participants had venous ropivacaine concentration values above 2.2 μg/mL. The highest ropivacaine concentration was 5.1 μg/mL, while only one patient had a small drop in arterial blood pressure [13]. Other trials observed that total venous ropivacaine concentration increased from 2.39 to 6.08 μg/mL during long-term epidural ropivacaine infusion, and even a value of 7.1 μg/mL was reported with no evidence of systemic toxicity events [14,15]. An experimental animal model draws a similar conclusion that it is not related to adverse electrophysiological or hemodynamic effects when ropivacaine concentration reaches potentially toxic levels [16]. In some cases, it is difficult to justify the correlation between local anesthetic concentrations and signs of systemic toxicity. This kind of relationship is multifactorial and influenced by individual conditions, such as anatomy and physiological state [17].

Many methods have been attempted to address chest tube pain, such as injections of local anesthetics into pleural or mediastinal drains, and even the application of lidocaine to chest tubes can relieve pain after cardiac surgery [18,19]. Several complications have been reported following these methods, including infection, pneumothorax, systemic absorption, and even ventricular standstill [20]. RSB targets upper abdominal postoperative analgesia and can solve chest tube related pain definitely and safely. In our study, only two patients complained of pain at chest tube site, which proved that PIFB combined with RSB is effective to offer better analgesia after cardiac surgery, meanwhile, it is relatively safe.

There are some limitations in this study. First, the sample size was small. Our study is merely exploratory to evaluate the safety of large volume fascial blocks in cardiac surgery patients. Although ten patients were enrolled, all ropivacaine concentration values were lower than the toxic thresholds. Second, PIFB and RSB were performed after induction to relieve patients' discomfort. Successful blocks were estimated by opioids and hemodynamics, not the definite sensory range of patients. While all regional blocks were finished under ultrasound, and spread of drugs was precisely observed.

Conclusions

We demonstrated that combined fascial plane blocks (PIFB & RSB) with a total injection of 70 mL 0.3% ropivacaine do not give rise to toxic levels, and PIFB combined with RSB is an effective and safe analgesic protocol for cardiac surgery patients.

Abbreviations

ASA, American Society of Anesthesiologists; AVR, aortic valve replacement; CABG, coronary artery by-

pass grafting; CPB, cardiopulmonary bypass; EF, ejection fraction; ICU, intensive care unit; LOS, length of stay; MVR, mitral valve replacement; NRS, numeric rating scale; PCIA, patient controlled intravenous analgesia; PIFB, pecto, intercostal fascial block; RSB, rectus sheath block.

Availability of Data and Materials

Datasets used for this study are available by the authors upon appropriate request.

Author Contributions

LJ and YF contributed to the study design and analysis. LW and BL performed the experiments and wrote the manuscript. BJ and YS assisted in the recruitment of participants and performed the statistical analysis. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of it.

Ethics Approval and Consent to Participate

This research was approved by Ethical Review Committee of Peking University People's Hospital (#2022PHB179-001). Written informed consent was obtained from all the patients.

Acknowledgment

Thanks Ting Hai, Zhou Zhao and Wei Yang for helpful discussion.

Funding

This work was funded by the National Key Research and Development Program of China (Grant No. 2018YFC2001905) and National Natural Science of Chian (Grant No. 8227051341).

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Lahtinen P, Kokki H, Hynynen M. Pain after cardiac surgery: a prospective cohort study of 1-year incidence and intensity. Anesthesiology. 2006; 105: 794–800.

[2] Jones J, Murin PJ, Tsui JH. Combined Pectoral-Intercostal Fascial Plane and Rectus Sheath Blocks for Opioid-Sparing Pain Control After Extended Sternotomy for Traumatic Nail Gun Injury. Journal of Cardiothoracic and Vascular Anesthesia. 2021; 35: 1551–1553.

[3] Toscano A, Balzani E, Capuano P, Vaninetti A, Perrucci C, Simonato E, *et al*. Awake cardiac surgery using the novel pectoralis-intercostal-rectus sheath (PIRS) plane block and subxiphoid approach. Journal of Cardiac Surgery. 2022; 37: 2923–2926.

[4] Kelava M, Alfirevic A, Bustamante S, Hargrave J, Marciniak D. Regional Anesthesia in Cardiac Surgery: An Overview of Fascial Plane Chest Wall Blocks. Anesthesia and Analgesia. 2020; 131: 127–135.

[5] Plakhotnik J, Zhang L, Estrada M, Coles JG, Lonnqvist PA, Maynes JT. Local Anesthetic Cardiac Toxicity Is Mediated by Cardiomyocyte Calcium Dynamics. Anesthesiology. 2022; 137: 687–703.

[6] Breindahl T, Simonsen O, Andreasen K. Column-switching HPLC-MS/MS analysis of ropivacaine in serum, ultrafiltrate and drainage blood for validating the safety of blood reinfusion. Journal of Chromatography. B, Analytical Technologies in the Biomedical and Life Sciences. 2010; 878: 76–82.

[7] Li M, Wan L, Mei W, Tian Y. Update on the clinical utility and practical use of ropivacaine in Chinese patients. Drug Design, Development and Therapy. 2014; 8: 1269–1276.

[8] Wu G, Sun B, Liu LI, Zhou J, Mo L, Ren C, *et al*. Lipid emulsion mitigates local anesthesia-induced central nervous system toxicity in rats. Experimental and Therapeutic Medicine. 2015; 10: 1133–1138.

[9] Schwoerer AP, Scheel H, Friederich P. A Comparative Analysis of Bupivacaine and Ropivacaine Effects on Human Cardiac SCN5A Channels. Anesthesia and Analgesia. 2015; 120: 1226–1234.

[10] Zausig YA, Zink W, Keil M, Sinner B, Barwing J, Wiese CHR, *et al*. Lipid emulsion improves recovery from bupivacaine-induced cardiac arrest, but not from ropivacaine- or mepivacaine-induced cardiac arrest. Anesthesia and Analgesia. 2009; 109: 1323–1326.

[11] Knudsen K, Beckman Suurküla M, Blomberg S, Sjövall J, Edvardsson N. Central nervous and cardiovascular effects of i.v. infusions of ropivacaine, bupivacaine and placebo in volunteers. British Journal of Anaesthesia. 1997; 78: 507–514.

[12] Bianconi M, Ferraro L, Traina GC, Zanoli G, Antonelli T, Guberti A, *et al*. Pharmacokinetics and efficacy of ropivacaine continuous wound instillation after joint replacement surgery. British Journal of Anaesthesia. 2003; 91: 830–835.

[13] Torup H, Mitchell AU, Breindahl T, Hansen EG, Rosenberg J, Møller AM. Potentially toxic concentrations in blood of total ropivacaine after bilateral transversus abdominis plane blocks; a pharmacokinetic study. European Journal of Anaesthesiology. 2012; 29: 235–238.

[14] Wiedemann D, Mühlnickel B, Staroske E, Neumann W, Röse W. Ropivacaine plasma concentrations during 120-hour epidural infusion. British Journal of Anaesthesia. 2000; 85: 830–835.

[15] Burm AG, Stienstra R, Brouwer RP, Emanuelsson BM, van Kleef JW. Epidural infusion of ropivacaine for postoperative analgesia after major orthopedic surgery: pharmacokinetic evaluation. Anesthesiology. 2000; 93: 395–403.

[16] Zaballos M, Varela O, Fernández I, Rodríguez L, García S, Quintela O, *et al*. Assessment of cardiotoxicity and plasma ropivacaine concentrations after serratus intercostal fascial plane block in an experimental model. Scientific Reports. 2023; 13: 47.

[17] Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept. Re-

gional Anesthesia and Pain Medicine. 2004; 29: 564–575; discussion 524.

[18] Cogan J, André M, Ariano-Lortie G, Nozza A, Raymond M, Rochon A, *et al*. Injection of Bupivacaine into the Pleural and Mediastinal Drains: A Novel Approach for Decreasing Incident Pain After Cardiac Surgery - Montreal Heart Institute Experience. Journal of Pain Research. 2020; 13: 3409–3413.

[19] Kang H, Chung YS, Choe JW, Woo YC, Kim SW, Park SJ, *et al*. Application of lidocaine jelly on chest tubes to reduce pain caused by drainage catheter after coronary artery bypass surgery. Journal of Korean Medical Science. 2014; 29: 1398–1403.

[20] Jagadeesan J, Kannan R, Dujon D. Ventricular standstill: a complication of intrapleural anesthesia using bupivacaine in a patient with free transverse rectus abdominus myocutaneous flap breast reconstruction. Annals of Plastic Surgery. 2007; 59: 445–446.