

**Plasma Ropivacaine Concentrations after
Ultrasound-guided Rectus Sheath Block in
Patients Undergoing Lower Abdominal Surgery**

Short Title : Ropivacaine concentration after rectus sheath blocks

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Abstract

A rectus sheath block can provide postoperative analgesia for midline incisions. However information regarding the pharmacokinetics of local anesthetics used in this block is lacking. In this study, we detail the time course of ropivacaine concentrations following this block. Thirty-nine patients undergoing elective lower abdominal surgery were assigned to three groups receiving rectus sheath block with 20mL of different concentrations of ropivacaine. Peak plasma concentrations (C_{max}) were dose-dependent, and there were no significant differences in the times (T_{max}) to C_{max} . The present data also suggested a slower absorption kinetics profile for ropivacaine following rectus sheath block than other compartment blocks.

Number of words: 100

Introduction

The rectus sheath block was first described by Schleich¹⁾ to provide relaxation of the anterior abdominal wall for intra-abdominal surgery. This block can also provide postoperative analgesia for procedures utilizing a midline incision²⁻⁶⁾ by acting on the terminal branches of the 7th-11th intercostal nerves within the rectus sheath, although it requires relatively high volume of local anesthetics. Recently, ultrasound-guided regional anesthesia and analgesia has improved the placement of local anesthetics and reduced inadvertent vessel or peritoneal puncture in pediatric patients⁷⁾. However, information regarding the potential for local anesthetic systemic toxicity with this block is lacking. In this study, we detail the pharmacokinetics of various concentrations of ropivacaine following rectus sheath block for lower abdominal surgery.

Methods

With the approval of our University ethics committee and written informed consent, 39 adult patients (ASA 1-2) undergoing elective lower abdominal surgery with midline incisions were enrolled into this study. Patients with bleeding tendency or coagulation disorder were excluded. Laparotomy was performed by the same surgical team. All patients were premedicated orally with diazepam 4-10 mg and roxatidine 75 mg 90 min before the induction of anesthesia. Anesthesia was induced with propofol 1-1.5mg/kg and fentanyl 100 µg. Following muscle relaxation with intravenous vecuronium 0.1mg/kg, endotracheal intubation was performed. Anesthesia was maintained with propofol 5-10 mg/kg/hr and fentanyl (total 10 µg/kg) along with an oxygen/air mixture ($FiO_2=0.4$). Muscle relaxation was maintained with vecuronium. Propofol infusion rate was altered to maintain the bispectral index (BIS) between 40 and 50 during anesthesia.

The patients were randomly assigned to three groups (n=13 each) receiving rectus sheath block with 20 mL of different concentrations of ropivacaine: 0.75 (Group 0.75), 0.5 (Group 0.5) and 0.25 % (Group 0.25) to determine pharmacokinetics. Following general anesthesia, a bilateral ultrasound-guided rectus sheath block was performed. Ten milliliters of the study drug solution was injected symmetrically on each side. We utilized a real-time and in-plane needle insertion technique in which the needle and spread of local anesthetic was fully visualized using a portable ultrasound unit and a 6-12MHz linear probe (MicroMaxx, SomoSite™, Bothell, WA, USA) (Figure 1). The injection was performed in the same manner on the opposite side.

To determine plasma concentrations of ropivacaine, arterial blood (3 mL) was drawn from a radial artery catheter before and 15, 30, 45, 60, 90, 120 and 180 min after completion of bilateral

rectus sheath blocks. Blood samples were centrifuged to separate the plasma, which was stored at -20°C until assay. Plasma ropivacaine concentrations were analyzed by gas chromatography with mass spectrometry (GC/MS) previously described by Björk et al ⁸⁾, with tetracaine as the internal standard. Tetracaine was only used as an internal standard, was not administered to patients. The retention times for tetracaine and ropivacaine were 4.9min and 4.7min, respectively. The limit of determination for ropivacaine was 10ng/mL. The within-day (intraassay) coefficient of variation of the assay varied from 3.7% at 500ng/mL to 3.1% at 1000ng/mL. Sample size of at least 12 patients per group was needed to have a power of 80%, a SD of 0.5µg/mL and significance at the two-sided 5% level, and on the basis of previous studies⁹⁾, we expected a difference in mean C_{max} of about 0.6µg/mL between each group. Data are presented as mean±SD. Statistical analysis was performed using two-way repeated measures ANOVA with Dunnett's post-hoc test.

Results

Patient characteristics were not different among the three groups (Table1). Changes in plasma ropivacaine concentrations for the first 180 min following ultrasound-guided rectus sheath block are shown in Figure 2.

The C_{max} was significantly different between groups 0.25 and 0.75 ($p < 0.001$), and 0.25 and 0.5 ($p < 0.05$), while there were no statistically significant differences in T_{max} among the groups (Table2). Serious adverse events were not observed following rectus sheath block in any patient. The highest individual plasma concentration was 2.88 µg/ml observed 45min after rectus sheath block with 0.75% ropivacaine.

Discussion

This is the first report of the pharmacokinetics of ropivacaine after rectus sheath block. In general, compartment blocks tend to show rapid absorption kinetics, because the absorption rate is relative to the vascularity of the tissue, concentration of local anesthetic and the spread of injected solution. In the present study, the times to peak concentration of ropivacaine following rectus sheath block was similar in duration to those of ilioinguinal/iliohypogastric nerve blocks reported previously¹⁰⁻¹²), but delayed compared to those of paravertebral block⁹), intercostal blocks¹³) and transversus abdominis plane block¹⁴⁻¹⁵). The rectus muscle is supplied by the supra- and infra- epigastric arteries. Although this represents a highly vascular area, the local anesthetic is actually deposited in the relatively avascular fascial plane posterior to the muscle. This location for the deposition of local anesthetic may contribute to the slow vascular uptake. The threshold concentration for critical ropivacaine toxicity is not well established. Several reports for severe cardiovascular toxicity (cardiac arrest, severe bradycardia etc.) after ropivacaine used have been documented, including measured plasma concentration data. In such cases of blood sampling, timing was within 45minutes after injection and plasma concentrations ranged from 3.2 to 3.6 $\mu\text{g}/\text{mL}$ ¹⁶⁻¹⁷). In this study, the highest individual plasma concentration was below this range. Furthermore most of our concentrations approach those associated with only mild CNS symptoms “levels ranging from 1 to 2 $\mu\text{g}/\text{mL}$, which were reported by Scott and colleagues¹⁸”. In conclusion, the present data demonstrated that plasma ropivacaine concentrations following ultrasound-guided rectus sheath block (0.25-0.75%; 20mL) increase dose dependently and do not reach critical toxic levels. Since the volume of the ropivacaine injection limited to 10mL per side and not based on mg/kg basis, the blood concentration data

reflecting the safety of this technique may not apply to patients with a larger body mass index than our study population.

Tables

Table 1. Patient characteristics.

	Ropivacaine group		
	0.25%	0.5%	0.75%
No of patients	13	13	13
Gender (Male/Female)	9/4	6/7	8/5
Age (y)	58[19-87]	59[37-76]	58[26-76]
Height (cm)	162±12	159±8	161±10
Weight (kg)	58±8	52±8	50±13
Duration of Surgery (min)	134±51	114±61	151±45

Data are expressed as Mean±S.D. or Mean[range]. There are no significant differences between groups.

Table 2. Maximum plasma concentration (C_{\max}) and time (T_{\max}) to reach C_{\max} after rectus sheath block with 0.75, 0.5 or 0.25% of ropivacaine.

	Ropivacaine group		
	0.25%	0.5%	0.75%
C_{\max} ($\mu\text{g}\cdot\text{mL}^{-1}$)	0.50±0.21	1.11±0.44*	1.51±0.82**
T_{\max} (min)	49.6±21.6	48.5±28.8	38.1±14.5

Mean±SD (n=13 per group).

*p<0.05, **p<0.01 compared with group 0.25%.

Figures and Illustrations

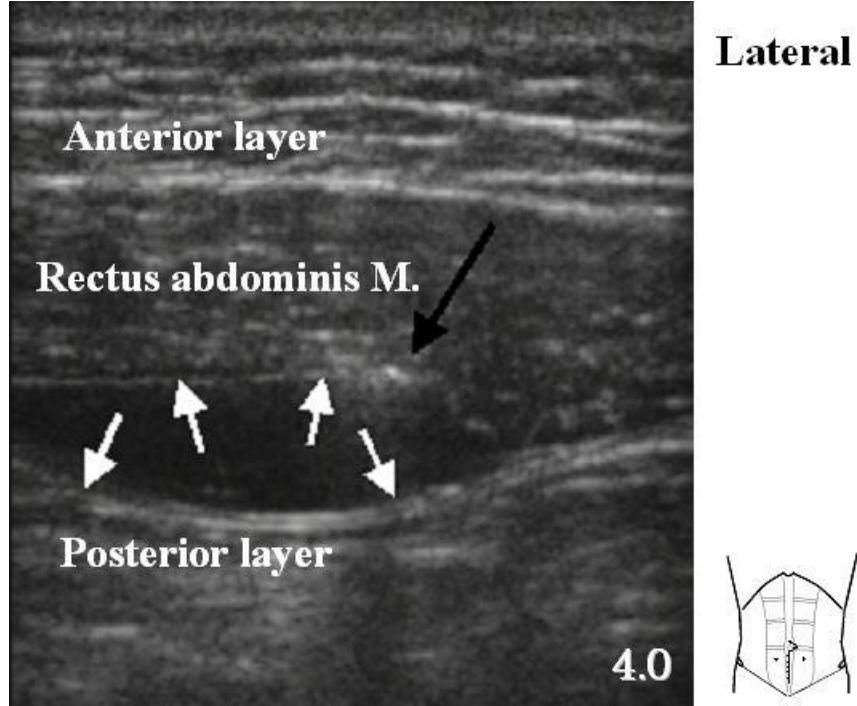


Figure 1. Wada M, et al.

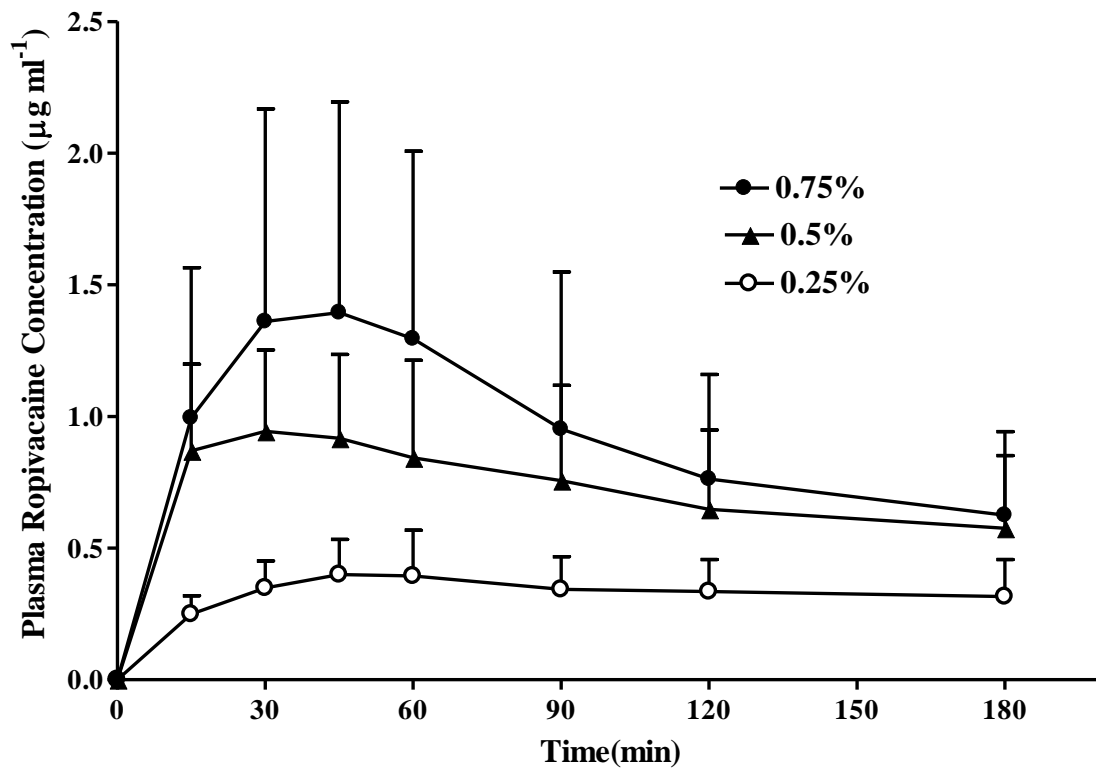


Figure 2. Wada M, et al

Figure Legends

Figure 1. Cross-sectional scan of rectus abdominis muscle during rectus sheath block. Injection sites were infra-umbilical (1-2cm below the umbilicus). White arrows indicate spread of the ropivacaine in the target, between the rectus abdominis muscle and the posterior sheath. Black arrow indicates the tip of the needle.

Figure 2. Mean arterial plasma concentration of ropivacaine after administration of 20ml of either 0.25, 0.5 or 0.75% ropivacaine for bilateral rectus sheath block. Data are presented mean \pm SD (n=13 per group)

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