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SHORT COMMUNICATION

Plasma ropivacaine concentration following ultrasound-guided subcostal transversus abdominis plane block in adults

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Abstract Ultrasound-guided subcostal transversus abdominis plane block (TAPB) is widely used for abdominal surgery; however, arterial plasma concentration of the anesthetic ropivacaine after the blockade is still unclear. We evaluated ropivacaine concentration after subcostal TAPB in adult patients undergoing upper abdominal surgery. Twelve patients with American Society of Anesthesiologists physical status 1–2 were enrolled. They received ultrasound-guided subcostal TAPB with 0.45 % ropivacaine at 3 mg/kg. Arterial plasma samples were collected at 15, 30, 45, 60, 90, and 120 min after the blockade and analyzed for total ropivacaine concentration using liquid chromatography and mass spectrometry. At every time point, the maximum concentrations (C_{max}), and time to the C_{max} (T_{max}) were recorded. The mean C_{max} and T_{max} were 1.87 (0.78) μg/ml and 31.3 (16.7) min, respectively. No adverse events or clinical symptoms indicating systemic toxicity were observed during this study. The study demonstrated that administration of ropivacaine at 3 mg/kg during subcostal TAPB led to rapid increases in plasma concentration of the anesthetic during the first 2 h after the blockade. C_{max} nearly reached the threshold for systemic toxicity.

Keywords Ultrasound · Transversus abdominis plane block · Ropivacaine

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Subcostal transversus abdominis plane block (TAPB) has been reported to provide effective postoperative analgesia for patients undergoing upper abdominal surgery [1]. The ultrasound-guided technique is routinely used for subcostal TAPB, and long-acting local anesthetic such as ropivacaine is often administered. One of the main concerns about this technique is the systemic toxicity of the local anesthetic, because subcostal TAPB requires a large dose and volume of local anesthetic. However, subcostal TAPB is often performed under general anesthesia and this may mask systemic symptoms of toxicity, even when the plasma concentration of the local anesthetic exceeds the safe limit.

Although ropivacaine, a long-acting local anesthetic, has been widely used for this blockade, its concentration in plasma after subcostal TAPB is still unclear. Only one report suggests that venous plasma concentration after posterior TAPB with ropivacaine at 3 mg/kg has potential for central nervous system toxicity [2]. Arterial plasma concentration is more reliable in assessing the toxic threshold than venous plasma concentration in general, because arterial blood carries the local anesthetic to various parts of the body [3]. This study is the first to investigate arterial plasma ropivacaine concentration following ultrasound-guided subcostal TAPB in adults.

After approval by the institutional ethics committee (Fukushima Prefectural Aizu General Hospital), written informed consent was obtained from 12 patients with American Society of Anesthesiologists physical status 1–2 who were scheduled for open upper abdominal surgery in our institution (Fukushima Prefectural Aizu General Hospital). Exclusion criteria were emergency surgery, liver or renal dysfunction, general contraindications for peripheral nerve block, history of allergy to amino-amido local anesthetics, or lack of informed consent.

General anesthesia was induced using a standardized protocol with 1–2 mg/kg of propofol, 0.3–0.5 μg/kg/min of remifentanil, and 0.6 mg/kg of rocuronium. Anesthesia was maintained with sevoflurane and 0.1–0.5 μg/kg/min of remifentanil. An indwelling peripheral arterial catheter was used for sample collection. After intubation of the trachea, ultrasound-guided bilateral subcostal TAPB was performed using 3 mg/kg of 0.45 % ropivacaine diluted with a commercially available 0.75 % solution. We scanned the abdominal wall along the subcostal margin near the midline following a previously reported method [4]. The ultrasound probe was moved laterally along the subcostal margin until the transversus abdominis muscle, internal oblique muscle, and external oblique muscle were identified by the ultrasound system (M-Turbo; Sonosite, Seattle, WA, USA). A 20-G Tuohy needle (Hakko, Nagano, Japan) was advanced laterally towards the neurofascial plane under long-axis (in-plane) ultrasound guidance. The local anesthetic was then injected with frequent aspiration to avoid intravascular injection. All patients received the blockade by a skilled anesthetist, and time duration from the first injection to the last was <5 min. Subsequently, ultrasound was used to confirm that the local anesthetic spread in a biconvex lens shape, which is indicative of correct injection in the TAP.

Arterial blood samples (5 ml) were collected from the indwelling arterial catheter at 15, 30, 45, 60, 90, and 120 min after the end of injection. Following centrifugation of these samples, plasma samples were temporarily stored in a refrigerator and transported in one batch to Shimadzu Techno-Research (Kyoto, Japan) for measurement of total plasma concentration of ropivacaine using liquid chromatography-tandem mass spectrometry (LC-MS/MS). The LC-MS/MS system consisted of high-performance liquid chromatography (Prominence HPLC System; Shimadzu, Kyoto, Japan) with an analyzer column (Inertsil ODS-3; GL Sciences, Tokyo, Japan), an MS/MS analysis system (API 3000-LC/MS/MS System; Applied Biosystems Japan, Tokyo, Japan), and analysis software (Life Technologies Japan, Tokyo, Japan). The peak plasma concentration of ropivacaine (C_{max}) and the time to C_{max} (T_{max}) were obtained directly from the observed data, which were summarized as mean (SD). In addition to the subcostal TAPB, intravenous flurbiprofen axetil (50 mg) was administered just before the end of the surgery, and patient-controlled intravenous fentanyl was used as part of a multimodal analgesic regimen. Adverse events were recorded from time of arrival at the operating room to discharge from the postoperative care unit.

The patients' demographic data are presented in Table 1, while changes in ropivacaine arterial plasma concentration in the individual patients are presented in Fig. 1. The mean C_{max} and T_{max} were 1.87 (0.78) μg/ml and 31.3 (16.7) min, respectively. No adverse events or clinical symptoms indicating systemic toxicity were observed during this study.

Table 1 Patient demographic data

Age (years)	65.3 (7.1)
Weight (kg)	55.3 (9.0)
Duration of surgery (min)	238.4 (71.2)
Duration of anesthesia (min)	311.4 (72.1)
Male:female	7:5

Data presented as mean (SD)

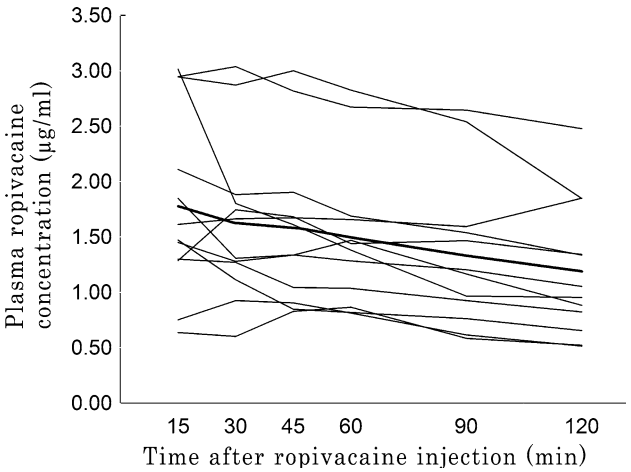

Fig. 1 *Black lines* indicate individual data. *Bold line* indicates mean data

Although previous investigations have reported relationships between peripheral nerve blocks other than subcostal TAPB and plasma ropivacaine concentration [5–7], this is the first report on changes in arterial plasma concentration of ropivacaine after ultrasound-guided subcostal TAPB. We noted rapid increases in plasma concentration of ropivacaine during the first 2 h after the injection, with the highest C_{max} nearly reaching toxic threshold.

The toxic threshold of ropivacaine has previously been reported. McCartney et al. [8] showed that 4.48 μg/ml of venous ropivacaine caused CNS toxicity in healthy premedicated volunteers. Knudsen et al. [9] reported 4.3 (0.6) μg/ml of arterial ropivacaine as the threshold for systemic toxicity. Another study indicated that venous plasma concentration reached potentially toxic levels after posterior TAPB with ropivacaine at 3 mg/kg [2]. However, venous plasma concentration is reported to be potentially unreliable, and arterial plasma concentration at an earlier time point may be underestimated because arterial blood delivers the local anesthetic to the brain and heart where the local anesthetic toxicity occurs. On the other hand, the

local anesthetic in venous plasma is residual after absorption by such parts of the body [3]. Therefore, arterial plasma concentration would be better suited to analyze the toxic threshold.

Our limitations were that we only measured total plasma concentration, whereas the toxicity of ropivacaine arises from the unbound fraction of ropivacaine, which was not measured because of the costs involved.

We only collected data after the 15 min post-injection, and the plasma concentration decreased in 7 of 12 patients during the first 30 min. Karmakar et al. reported an arterial and venous pharmacokinetic difference following thoracic paravertebral block with ropivacaine. They presented more rapid increases of arterial plasma concentration than venous and highlighted the importance of arterial blood sampling in assessing local anesthetic toxicity [3]. Their results indicate that our data do not correctly reflect the true peak plasma concentration. The true peak may be observed earlier than 15 min post-injection in subcostal TAPB.

In conclusion, we demonstrated that administration of ropivacaine at 3 mg/kg for subcostal TAPB led to rapid increases in plasma concentration of the anesthetic during the first 2 h after the blockade. The highest C_{max} nearly reached the threshold for systemic toxicity. However, the time course during the first 15 min requires further study.

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