Original Article
Perineuraxial dexmedetomidine decreases the minimum effective volume of ropivacaine for ultrasound-guided supraclavicular brachial plexus block

Xiaowei Qian, Hang Zhao, Yuquan Rao, Yang Nan, Zhongsu Wang, Xiaoqing Wang, Qingquan Lian, Jun Li

Department of Anesthesiology, Critical Care and Pain Medicine, The Second Affiliated Hospital & Yuying Children Hospital of Wenzhou Medical University, Wenzhou, China

Received May 15, 2016; Accepted September 7, 2016; Epub October 15, 2016; Published October 30, 2016

Abstract: Dexmedetomidine is a selective α-2-adrenoceptor agonist which might be used as a local anesthetic (LA) adjuvant for peripheral nerve block. Previous study had showed that dexmedetomidine could suppress the peak amplitude of Na⁺ current in neuronal cells. We designed this study to determine the minimum effective volume (MEV) of ropivacaine with or without dexmedetomidine for ultrasound-guided supraclavicular brachial plexus block (SBPB), to quantify the sparing effect of dexmedetomidine on the MEV of ropivacaine. Thirty-four adult patients scheduled for forearm and hand surgeries under supraclavicular brachial plexus block were randomized into two groups: Group R (0.75% ropivacaine) and Group RD (0.75% ropivacaine plus dexmedetomidine). A successful block was defined as complete loss of cold sensation at the sensory dermatomes of four main nerves within 45 min after completed LA injection. The MEV of ropivacaine with or without dexmedetomidine was determined by using up-and-down method introduced by Dixon and Massey. The MEV for 0.75% ropivacaine was 15.5 ml [confidence interval 95% (CI): 13.9-17.2 ml] in Group R vs. 14.0 ml (95% CI: 12.5-15.6 ml) in Group RD. Dexmedetomidine 30 µg decreased the MEV of ropivacaine by about 10%. Systolic arterial blood pressure and heart rate levels were lower in group RD than in group R, and sedation level was higher in group RD than in group R. There were no differences in the incidence of paraesthesia, nerve stimulation, vascular puncture, and bradycardia. Perineuraxial dexmedetomidine 30 µg produced a 10% reduction of MEV of ropivacaine for ultrasound-guided SBPB.

Keywords: Anesthetic techniques, regional, brachial plexus, anesthetics local, ropivacaine, equipment, ultrasound machines

Introduction

The supraclavicular brachial plexus block (SBPB) is commonly used to provide anesthesia for forearm and hand surgery. Large volumes of long-acting local anesthetic (LA) were usually chosen to improve the success rate and prolong the duration of brachial plexus block, which may resulted in increasing the risk of systemic toxicity. Ultrasound guidance was then invented to provide a successful peripheral nerve block by using a small volume of LA.

Dexmedetomidine, a selective α-2-adrenoceptor agonist, as a local anesthetic (LA) adjuvant has been shown to prolong the duration of analgesia in a series of preclinical and clinical studies [1-8]. One preclinical study showed that dexmedetomidine suppressed the peak amplitude of Na⁺ current in neuronal cells [9]. For LAs suppress nerve excitability and exert clinical effects through the blockade of Na⁺ channel [10], exposure to dexmedetomidine can produce inhibitory effects on Na⁺ channel currents and may thus be potential mechanisms through which it may depress neuronal excitability [9]. This finding indicates that perineuraxial dexmedetomidine as an adjuvant might have a LA effect and decrease the LA requirement during brachial plexus block. However, this effect has not yet been investigated in clinical study.

The primary objective of the present study is to investigate whether perineuraxial dexmedetomidine as an adjuvant could decrease the mini-
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Mum effective volume (MEV) of ropivacaine required for ultrasound-guided SBPB.

Methods

The present study was approved by the ethical committee of the Second Affiliated Hospital of Wenzhou Medical University and registered at Chinese Clinical Trials.gov (ChiCTR-OOC-1500-5869). After obtained written informed consent from all patients, thirty-four patients (ASA physical status I or II, aged from 18 to 65 years) scheduled for forearm and hand surgeries under SBPB were enrolled in this prospective, randomized, double-blinded study. Exclusion criteria were patients who receiving adrenoreceptor antagonist or agonist therapy, allergic to LAs, a current brachial plexus injury, infection at the puncture site, and unable to provide informed consent; those with a history of morbid obesity (body mass index >35 kg/m²), hypertension, diabetes, chronic pain, and pregnant women.

No premedication was given before SBPB. All patients had an intravenous catheter inserted into the vein of nonoperated arm and Lactated Ringer’s solution administered at 5 ml/kg/h. Pulse oximetry (SpO₂), electrocardiogram (ECG), and non-invasive arterial pressure (NIBP) were recorded before the block was performed. According to Gupta et al. [11], the Ultrasound-guided SBPB was carried out by a single operator who had considerable experience with this method. After sterile preparation of the probe and disinfection of the skin, a Sonosite M-Turbo (Sonosite, Inc., Bothell, WA, USA) with a 13-MHz linear probe was used to visualize the structures of the brachial plexus in the supraclavicular region. After a subcutaneous infiltration with 1% lidocaine, a 50-mm, 22-gauge needle (Stimuplex A, B.Braun, Havel’s, Cincinnati, OH) was directed to the plexus under ultrasound guidance using in-plane technique. Before injection of LA, the needle tip position was identified by injecting 0.5 ml bolus of saline. After aspiration, the prepared LA injection containing 0.75% ropivacaine (AstraZeneca, Södertälje, Sweden) (Group R) or 0.75% ropivacaine with 0.3 ml (30 µg) dexmedetomidine (Jiangsu Hengrui Medicine Co., Ltd, Liyang, China) (Group RD) was then deposited. Using six-injection technique, we ensure the upper, middle, and lower trunks of the plexus were surrounded with LA solution.

The patients were randomly allocated to one of the two groups by an anesthesiologist not involved in the study using sealed envelopes: Group R (0.75% ropivacaine, n = 17) and Group RD (0.75% ropivacaine plus dexmedetomidine, n = 17). The LA injections were prepared and then covered with nontransparent stickers by the same anesthesiologist not involved in the study. The volume of LA injection for consecutive patients was determined according to the block effect of the previous patient. Based on our experience, the initial volume of ropivacaine was 21 ml in Group R and 18 ml in Group RD was expected to be sufficient for most patients. The increment or decrement was set as 1.5 ml for both groups. A successful or a failed block determined, respectively, a 1.5 ml volume reduction or increase for the next patient.

An investigator blinded for the block conduct and the injected volume assessed each block. Using cold sensation test, the efficacy of the block was assessed at 5-min intervals for up to 45 min. The endpoint of a success or a failure of the block was defined according to Gupta et al [11]. A successful block was defined as complete loss of cold sensation at the sensory dermatomes of the ulnar, median, radial, and musculocutaneous nerves within 45 min after completed LA injection. Failure to achieve complete loss of cold sensation at any of the four sensory dermatomes after 45 min after completed LA injection was considered a failed block. The block was also deemed a failed block if the patient complained of pain during surgery, despite the complete loss of cold sensation. For patients with failed block, a supplemental peripheral nerve blocks, intravenous fentanyl intraoperatively or general anesthesia was administrated as appropriate to achieve surgical analgesia.

Systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), heart rate (HR), and SpO₂ were recorded at baseline, 5 min, 10 min, 15 min, 30 min, 45 min, 60 min, 90 min, and 120 min. Adverse events comprised hypotension (defined as a 30% decrease in relation to the baseline), bradycardia (defined as HR < 50 beats per minute), respiratory depression (defined as SpO₂ < 90%), or nausea and vomiting. We also recorded the paraesthesia, nerve stimulation, vascular puncture, and systemic
toxicity to LA during the block procedure. Sedation was evaluated by a 4-point scale (1 = awake and nervous, 2 = awake and calm, 3 = sleepy and easily arousal, 4 = sleepy and difficultly to rouse).

Statistics and power analysis

Using the formula by Dixon and Massey [12], sample size (N) was calculated as follows: Briefly, N = 2(SD/SEM)^2 where SD represents standard deviation and SEM the standard error of the mean. A sample size of 15 subjects in each group is needed for the study, assuming a 4 ml SD and 1.5 ml SEM. We assigned 17 patients to each of the two groups, anticipating a dropout rate of 10%.

The MEV of ropivacaine was estimated using up-and-down method introduced by Dixon and Massey [11]. Statistical analysis was performed with SPSS 16.0 for windows (SPSS Inc., Chicago, IL). Normality of distribution was evaluated using the Kolmogorov-Smirnov test. Normally distributed data are presented as mean (SD). Categorical data are presented as n or n (%). Normally distributed data between two groups were analyzed using independent 2-sample t test. Repeat measured ANOVA was used for measurement with multiple time points.

Categorical data were analyzed using the method of χ² test or Fisher exact test. A value of P < 0.05 was considered as statistically significant.

Results

The patients were recruited from May 2015 to Oct 2015. A total of 34 subjects completed the study and were included in the final analysis (Figure 1). Characteristics and surgical data were similar between the two groups (Table 1). The sequence of successful and failed blocks is shown in Figure 2. The MEV for 0.75% ropivacaine was calculated using Dixon’s formula to be 15.5 ml [confidence interval 95% (CI): 13.9-17.2 ml]. The MEV for 0.75% ropivacaine with dexmedetomidine 30 µg was calculated using Dixon’s formula to be 14.0 ml (95% CI: 12.5-15.6 ml). Dexmedetomidine 30 µg decreased the MEV of ropivacaine by about 10%.

In group R, out of 6 failed blocks, 2 of these 6 patients required supplemental peripheral nerve block and 4 patients received intravenous fentanyl intraoperatively. In group RD, out of 7 failed blocks, 3 of these 7 patients required supplemental peripheral nerve block and 4 patients received intravenous fentanyl intraoperatively. The amounts of fentanyl used were similar between the two groups. None of these patients received general anesthesia.

Adverse events are listed in Table 2. No significant differences between the two groups were reported regarding the incidence of paraesthesia, nerve stimulation, vascular puncture, and bradycardia. More patients were sleepy but easily arousable in group RD than in group R (P = 0.001). No adverse events including systemic toxicity to LA, hypotension, respiratory depression, nausea, and vomiting were observed in either group. SAP levels in group RD at 30 and 45 minutes were significantly lower than those in group R (P < 0.05; Figure 3). DAP levels were similar between the two groups. HR level in group RD at 30 minute was significantly lower than that in group R (P < 0.05; Figure 4).

Discussion

In this prospective, triple-blinded, randomized, and up-down sequential allocation trial, we
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found the MEV of 0.75% ropivacaine required for ultrasound-guided SBPB using Dixon's formula to be 15.5 ml (95% CI: 13.9-17.2 ml), whereas the MEV of 0.75% ropivacaine with dexmedetomidine 30 µg using the same formula was 14.0 ml (95% CI: 12.5-15.6 ml). Perineuraxial dexmedetomidine 30 µg decreased the MEV of ropivacaine for ultrasound-guided SBPB by about 10%.

Several trials using LA coadministered with dexmedetomidine have been reported, of which the dose of dexmedetomidine ranged from 20 to 150 µg [1-4]. Esmaoglu et al [4], have found that perineuraxial dexmedetomidine 100 µg may lead to bradycardia, whereas dexmedetomidine 20 µg have not [3]. We used dexmedetomidine 30 µg for the present study and the assumption that bradycardia will not occur with this dose.

Several preclinical studies showed that dexmedetomidine as an adjuvant added to LAs could enhance sensory blockade for peripheral nerve block [5-8]. In addition, several off-label clinical trials also found that dexmedetomidine as an adjuvant to LA could prolongs peripheral nerve block [1-4]. Previous studies, however, did not investigate whether peri-neuraxial dexmedetomidine has a LA effect and quantify the sparing effect of dexmedetomidine on LA requirement during brachial plexus block. In our present study, we found that dexmedetomidine 30 µg as an adjuvant decreased the MEV of ropivacaine for ultrasound-guided SBPB by about 10%, which suggests that dexmedetomidine as an adjuvant might has a LA effect.

The mechanism by which dexmedetomidine has a LA effect is not elucidated. LAs exert cli-

Table 1. Patient characteristics and surgical data

<table>
<thead>
<tr>
<th></th>
<th>Group R</th>
<th>Group RD</th>
<th>T</th>
<th>χ²</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), years</td>
<td>38.7 (10.3)</td>
<td>35.8 (10.0)</td>
<td>0.842</td>
<td>0.515</td>
<td>0.406</td>
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<td>Gender (male/female), n</td>
<td>10/7</td>
<td>12/5</td>
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<td></td>
<td>0.473</td>
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<tr>
<td>Height, mean (SD), cm</td>
<td>167.8 (8.1)</td>
<td>169.9 (6.7)</td>
<td>0.834</td>
<td>0.301</td>
<td>0.765</td>
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<td>Weight, mean (SD), kg</td>
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<td>61.8 (10.6)</td>
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<td></td>
<td>0.656</td>
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<td>ASA physical status (I/II), n</td>
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<td></td>
<td></td>
<td>0.776</td>
</tr>
<tr>
<td>Surgery duration, mean (SD), min</td>
<td>85.3 (50.3)</td>
<td>89.7 (38.4)</td>
<td>0.288</td>
<td></td>
<td>1.000</td>
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<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Finger/wrist arthroplasty, n</td>
<td>2/1</td>
<td>3/2</td>
<td></td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Finger/wrist ORIF, n</td>
<td>10/2</td>
<td>9/1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radius/ulnar ORIF, n</td>
<td>1/1</td>
<td>2/0</td>
<td></td>
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</tr>
</tbody>
</table>

Continuous variables are expressed as mean (SD). Continuous variables were analyzed using independent 2-sample t test. Categorical variables are expressed as counts. Categorical data were analyzed using the method of χ² test (gender) or Fisher exact test (other categorical variables). SD, standard deviation; ASA, American Society of Anesthesiologists; ORIF, open reduction-internal fixation.

Figure 2. A. The minimum effective volume (MEV) of 0.75% ropivacaine required for ultrasound-guided supraclavicular brachial plexus block (SBPB) is 15.5 ml [confidence interval 95% (CI): 13.9-17.2 ml] using the formula of Dixon and Massey. The testing interval is 1.5 ml. The horizontal dashed line represents the MEV of 0.75% ropivacaine, 15.5 ml. B. The MEV for 0.75% ropivacaine with dexmedetomidine 30 µg is 14.0 ml (95% CI: 12.5-15.6 ml) using the formula of Dixon and Massey. The testing interval is 1.5 ml. The horizontal dashed line represents the MEV of 0.75% ropivacaine, 14.0 ml.
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Table 2. Adverse events

<table>
<thead>
<tr>
<th></th>
<th>Group R</th>
<th>Group RD</th>
<th>χ²</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paraesthesia, n (%)</td>
<td>4 (23.5)</td>
<td>3 (17.6)</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>Nerve stimulation, n (%)</td>
<td>2 (11.8)</td>
<td>2 (11.8)</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>Vascular puncture, n (%)</td>
<td>1 (5.9)</td>
<td>0 (0)</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>Bradycardia, n (%)</td>
<td>0 (0)</td>
<td>1 (5.9)</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>Max sedation level 1-2-3-4 (n)</td>
<td>12-5-0-0</td>
<td>1-7-9-0</td>
<td>15.07</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Categorical variables are expressed as counts (percentage) except maximum sedation level which are number of patients. Categorical data were analyzed using the method of χ² test (max sedation level) or Fisher exact test (other categorical variables). *χ² P = 0.001. SD, standard deviation.

Figure 3. Systolic and diastolic arterial pressure time course. Asterisks indicate individual time points in which SAP levels in group RD were significantly lower than those in group R (P < 0.05). R, ropivacaine; RD, ropivacaine plus dexmedetomidine; SAP, systolic arterial blood pressure; DAP, diastolic arterial blood pressure.

through the channels and Na⁺ current [13, 14]. Chen and colleagues found that dexmedetomidine significantly depressed Na⁺ currents in cultured cerebellar neurons, which indicated that dexmedetomidine might affect neuronal activity in vivo [9].

Some studies reported that perineural dexmedetomidine could decrease blood pressure and heart rate [2, 4, 15]. We used 30 µg perineural dexmedetomidine and also found that SAP levels at 30 and 45 minutes were significantly lower in dexmedetomidine group when compared with the ropivacaine group. HR level at 30 minutes was significantly lower in dexmedetomidine group than that in ropivacaine group. However, we did not found that perineural dexmedetomidine increased the incidence of hypotension and bradycardia. We think that dexmedetomidine-induced adverse effects such as hypotension and bradycardia are likely to be dependent on the total dose. Esmaoglu et al [4] found that perineural dexmedetomidine 100 µg added to levobupivacaine for axillary brachial plexus block may lead to bradycardia. Fritsch et al [2] used perineural dexmedetomidine 150 µg added to ropivacaine for interscalene block and also found that bradycardia was more frequent in dexmedetomidine group. However, peri-neural dexmedetomidine 20 µg was not result in significant bradycardia [3].

One previous study had showed that neuraxial dexmedetomidine could cause sedation [16]. Another study reported that peri-neural dexmedetomidine-associated sedation increased in a dose-dependent manner [17]. Our results also indicated that more patients were sleepy...
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In conclusion, the addition of dexmedetomidine 30 µg decreased the MEV of ropivacaine for ultrasound-guided SBPB by about 10%, with a higher sedation level when compared with ropivacaine alone. Perineural dexmedetomidine 30 µg did not increase the incidence of hypotension and bradycardia. Our results encourage the use of perineural dexmedetomidine as an adjuvant for patients undergoing peripheral nerve block.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Jun Li, Department of Anesthesiology, Critical Care and Pain Medicine, The Second Affiliated Hospital & Yuying Children Hospital of Wenzhou Medical University, Wenzhou, China. Tel: 86-577-88002927; Fax: 86-577-8800-2925; E-mail: lijunwzmu@126.com

References


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