A Multicenter Randomized Comparison Between Intravenous and Perineural Dexamethasone for Ultrasound-Guided Infraclavicular Block

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Background and Objectives: This multicenter, randomized trial compared intravenous (IV) and perineural (PN) dexamethasone for ultrasound (US)-guided infraclavicular brachial plexus block. Our research hypothesis was that modalities would result in similar durations of motor block.

Methods: One hundred fifty patients undergoing upper limb surgery with US-guided infraclavicular block were randomly allocated to receive IV or PN dexamethasone (5 mg). The local anesthetic agent (35 mL of lidocaine 1%-bupivacaine 0.25% with epinephrine 5 μg/mL) was identical in all subjects. Patients and operators were blinded to the nature of IV and PN injectates. During the performance of the block, the performance time, number of needle passes, procedural pain, and complications (vascular puncture, paresthesia) were recorded.

Subsequently, a blinded observer assessed the success rate (defined as a minimal sensorimotor composite score of 14 of 16 points at 30 minutes), onset time as well as the incidence of surgical anesthesia (defined as the ability to complete surgery without local infiltration, supplemental blocks, IV opioids, or general anesthesia). Postoperatively (at 24 hours), the blinded observer contacted patients with successful blocks to enquire about the duration of motor block, sensory block, and postoperative analgesia. The main outcome variable was the duration of motor block.

Results: No intergroup differences were observed in terms of technical execution (performance time/number of needle passes/procedural pain/complications), onset time, success rate, and surgical anesthesia. However, compared to its IV counterpart, PN dexamethasone provided 19% to 22% longer durations for motor block (15.7 ± 6.2 vs 12.9 ± 5.5 hours; P = 0.009), sensory block (16.8 ± 4.4 vs 13.9 ± 5.4 hours; P = 0.002), and postoperative analgesia (22.1 ± 8.5 vs 18.6 ± 6.7 hours; P = 0.014).

Conclusions: Compared with its IV counterpart, PN dexamethasone (5 mg) provides a longer duration of motor block, sensory block, and postoperative analgesia for US-guided infraclavicular block. Future dose-finding studies are required to elucidate the optimal dose of dexamethasone.

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Dexamethasone can prolong the duration of interscalene, supraclavicular, and axillary brachial plexus blocks. Postulated mechanisms include inhibition of nociceptive C fibers, suppression of ectopic neural discharge, peripheral/central antiinflammatory effects, and suppression of the neuropeptide immune response to injury. The optimal route of administration remains controversial. Although some trials report longer analgesia with perineural (PN) compared to intravenous (IV) dexamethasone, other studies have failed to detect significant differences between the 2 modalities.

In this trial, we set out to compare IV and PN dexamethasone for ultrasound (US)-guided infraclavicular brachial plexus blocks (ICBs). As a precautionary measure, we designed the study as an equivalency trial and hypothesized that both modalities would result in similar durations. Because analgesic and sensory duration can be influenced by postoperative pain medications and trauma to small cutaneous nerves, respectively, we selected duration of motor block as the primary outcome.

METHODS

The current trial was registered at www.clinicaltrials.gov (study ID: NCT02150624001) on June 24, 2015. After obtaining ethics committee approval (McGill University Health Center, Montreal, Quebec, Canada; Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand; and Ramathibodi Hospital, Bangkok, Thailand) and written informed consent, we enrolled 150 patients undergoing surgery of the forearm, wrist, or hand. Inclusion criteria were age between 18 and 80 years, American Society of Anesthesiologists physical status I to III, and body mass index between 18 and 35 kg/m². Exclusion criteria were inability to consent to the study, coagulopathy, sepsis, hepatic or renal failure, allergy to local anesthetic (LA), preexisting muscularcuteaneous/median/radial/ulnar neuropathy, and prior surgery in the infraclavicular fossa.

After arrival in the induction room, an 18- or 20-gauge IV catheter was placed in the upper limb contralateral to the surgical site and IV premedication (0.015–0.03 mg/kg of midazolam and 0.6 μg/kg of fentanyl) was administered to patients if necessary. Supplemental oxygen (nasal cannulae at 4 L/min) and pulse oximetry were applied throughout the procedure.

The ICB was performed according to a previously described technique. The 6- to 13-MHz linear US probe (Sonosite M-Turbo; Sonosite Inc, Bothell, Washington) was applied in a sterile fashion in the infraclavicular fossa, medially to the coracoid process, in order to obtain a short axis view of the axillary artery. A skin wheal was raised with 3 mL of lidocaine 1%. Using an inline plane technique and a cephalad to caudad direction, a 22-gauge, 9-cm block needle (StimuQuick Echo; Arrow International Inc, Reading, Pennsylvania) was advanced until the tip was located dorsal to the axillary artery. Thirty-five milliliters of lidocaine 1%-bupivacaine 0.25% (obtained by mixing equal parts of lidocaine 2% and bupivacaine 0.5%) with epinephrine 5 μg/mL was incrementally injected. All blocks were performed by residents, fellows, or staff anesthesiologists. Independently of their status,
operators were considered experts if, before the start of the study, they possessed an experience level equal or superior to 60 ICBs. Otherwise, they were considered trainees.

Using a computer-generated sequence of random numbers and a sealed envelope technique, patients were randomly allocated to receive IV or PN dexamethasone (5 mg). Randomization was independently carried out in each of the 3 centers. In the PN group, 0.5 mL of dexamethasone (10 mg/mL) was administered with the LA and 0.5 mL of normal saline was injected intravenously. Conversely, in the IV group, 0.5 mL of normal saline was administered with the LA and 0.5 mL of dexamethasone (10 mg/mL) was injected intravenously. The study solutions were prepared by an investigator not involved in clinical care so patients and operators remained blinded to the nature of IV and PN injectates.

For both groups, the imaging time was defined as the time interval between contact of the US probe with the patient and the acquisition of a satisfactory picture. The needling time (defined as the temporal interval between the start of the skin wheal and the end of LA injection through the block needle) was also recorded. Thus, performance time was defined as the sum of imaging and needling times. The number of needle passes was also recorded. The initial needle insertion counted as the first pass. Any subsequent needle advancement that was preceded by a retraction of at least 10 mm counted as an additional pass. Furthermore, the level of procedural pain (0 = no pain; 10 = worst, imaginable pain) as well as the incidence of vascular puncture and paresthesia were recorded.

After LA injection through the block needle, measurements of brachial plexus blockade were carried out every 5 minutes until 30 minutes by a blinded observer. Sensory blockade of the musculocutaneous, median, radial, and ulnar nerves was graded according to a 3-point scale using a cold test: 0 = no block, 1 = analgesia (patient can feel touch, not cold), and 2 = anesthesia (patient cannot feel touch). Sensory blockade of the musculocutaneous, median, radial, and ulnar nerves were assessed on the lateral aspect of the forearm, the volar aspect of the thumb, the lateral aspect of the dorsum of the hand, and the volar aspect of the fifth finger, respectively. Motor blockade was also graded on a 3-point scale: 0 = no block, 1 = paresis, and 2 = paralysis. Motor blockade of the musculocutaneous, radial, median, and ulnar nerves were evaluated by elbow flexion, thumb abduction, thumb opposition, and thumb adduction, respectively. Overall, the maximal composite score was 16 points. We considered the block a success and the patient ready for surgery when a minimal composite score of 14 points was achieved, provided the sensory block score was equal or superior to 7 of 8 points. This scale has been used in previous studies. The onset time was defined as the time required to obtain 14 points. If, after 30 minutes, the composite score was inferior to 14 points, the patient was transferred to the operating room for the start of the surgery. For these patients, we did not record an onset time. Surgical anesthesia was recorded by the same blinded observer and defined as the ability to proceed with surgery without the need for IV narcotics, general anesthesia, rescue blocks, or LA infiltration by the surgeon. However, in case of anxiety (as voiced by patients or determined by the treating anesthesiologists), subjects could receive a propofol infusion (25–80 μg/kg per minute) intraoperatively, provided response to verbal stimulus was maintained. The blinded observer also recorded the patient's anthropometric data.

FIGURE 1. CONSORT diagram of patient flow through the study. Onset times could not be recorded for patients with minimal composite scores inferior to 14 points at 30 minutes. However, the performance time, number of needle passes, procedural pain, operator's experience level, adverse events (vascular puncture/paresthesia), and surgical anesthesia were recorded for these subjects. BMI, Body mass index.

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Postoperatively, patients with successful blocks (minimal composite score of 14 points at 30 minutes) were provided a data sheet to record the exact time when they first regained sensation in the fingers (duration of sensory block), moved the fingers (duration of motor block), and experienced pain at the surgical site (analgesic duration). We did not seek sensation or movement of specific digits but only of those whose tips were not covered by the cast. The blinded observer contacted study subjects at 24 hours for data collection. In the event that patients could not be reached or that ICBs had receded during sleep, we did not record any data for the duration of sensorimotor block and postoperative analgesia. However, data pertaining to technical execution/onset/success/surgical anesthesia were retained for analysis (Fig. 1).

One week after the surgery, patients were contacted by the blinded investigator to inquire about complications such as persistent numbness/paresthesia or motor deficit.

**Statistical Analysis**

In a preliminary pilot study, our experience with PN dexamethasone (5 mg) for US-guided ICB revealed a motor block duration of 802 ± 258.42 minutes. We deemed that a 25% difference in duration (200.5 minutes, ie, 3.3 hours) carries little clinical significance. Thus, a calculated sample size of 45 patients per group was required for a statistical power of 0.90 and a type I error of 0.025. Since block duration can only be calculated for successful blocks and because we anticipated a 90% success rate with a 35-mL volume,20 50 subjects per group were needed to compensate for block failure. Because the duration of motor block cannot be accurately measured if the patient cannot be contacted postoperatively or if the block wears off during the patient’s sleep, we elected to recruit an additional 25 subjects per group to account for possible dropout. Thus, a total of 150 patients were enrolled across the 3 centers.

Statistical analysis was performed using SPSS version 21 statistical software (IBM, Armonk, New York). For continuous data, normality was first assessed with the Lilliefors test and then analyzed with the Student t test. Data that did not have a normal distribution, as well as ordinal data, were analyzed with the Mann–Whitney U test. For categorical data, the χ2 or Fisher exact test was used. The log-rank test was used to analyze the Kaplan–Meier plots for duration of analgesia, sensory, and motor

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**TABLE 1. Patient Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>IV Dexamethasone (n = 75)</th>
<th>PN Dexamethasone (n = 75)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>42.5 ± 15.5</td>
<td>45.7 ± 15.1</td>
<td>0.134</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>49/26</td>
<td>35/40</td>
<td>0.032</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.4 ± 3.8</td>
<td>24.8 ± 4.4</td>
<td>0.480</td>
</tr>
<tr>
<td>ASA physical status</td>
<td>56/17/2</td>
<td>44/30/1</td>
<td>0.052</td>
</tr>
<tr>
<td>Types of surgery</td>
<td>40/27/6/2</td>
<td>38/24/10/3</td>
<td>0.600</td>
</tr>
</tbody>
</table>

Continuous variables are presented as means ± SD; categorical variables are presented as counts.

ASA indicates American Society of Anesthesiologists; BMI, body mass index.

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**TABLE 2. Block Performance Data**

<table>
<thead>
<tr>
<th></th>
<th>IV Dexamethasone (n = 75)</th>
<th>PN Dexamethasone (n = 75)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging time, s</td>
<td>29.2 ± 26.5</td>
<td>37.5 ± 38.2</td>
<td>0.045</td>
</tr>
<tr>
<td>Needling time, min</td>
<td>4.5 ± 2.0</td>
<td>4.8 ± 2.3</td>
<td>0.449</td>
</tr>
<tr>
<td>Performance time, min</td>
<td>5.0 ± 2.2</td>
<td>5.4 ± 2.5</td>
<td>0.253</td>
</tr>
<tr>
<td>Onset time, min</td>
<td>18.0 ± 6.9</td>
<td>17.1 ± 6.3</td>
<td>0.483</td>
</tr>
<tr>
<td>Total anesthesia-related time, min</td>
<td>23.1 ± 6.9</td>
<td>22.5 ± 6.7</td>
<td>0.643</td>
</tr>
<tr>
<td>Blocks with a minimal composite score of 14 points</td>
<td>65 (86.7)</td>
<td>66 (88.0)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Surgical anesthesia</td>
<td>71 (94.7)</td>
<td>74 (98.7)</td>
<td>0.367</td>
</tr>
<tr>
<td>Operator's experience level (expert/trainee)</td>
<td>24/51</td>
<td>23/52</td>
<td>0.867</td>
</tr>
<tr>
<td>No. passes</td>
<td>1 [1–7]</td>
<td>2 [1–5]</td>
<td>0.673</td>
</tr>
<tr>
<td>Block-related pain (scale 0–10)</td>
<td>0 [0–7]</td>
<td>1 [0–8]</td>
<td>0.180</td>
</tr>
<tr>
<td>Duration of motor block, h;</td>
<td>12.9 ± 5.5</td>
<td>15.7 ± 6.2</td>
<td>0.009</td>
</tr>
<tr>
<td>95% CI of the difference of the means</td>
<td>–4.9 to –0.72</td>
<td>–4.6 to 1.06</td>
<td>0.002</td>
</tr>
<tr>
<td>Duration of sensory block, h;</td>
<td>13.9 ± 5.4</td>
<td>16.8 ± 4.4</td>
<td>–4.58 to –1.06</td>
</tr>
<tr>
<td>95% CI of the difference of the means</td>
<td>–4.59 to –1.06</td>
<td>0.014</td>
<td></td>
</tr>
<tr>
<td>Duration of postoperative analgesia, h;</td>
<td>18.6 ± 6.7</td>
<td>22.1 ± 8.5</td>
<td></td>
</tr>
<tr>
<td>95% CI of the difference of the means</td>
<td>–5.9 to –0.45</td>
<td>&gt;0.999</td>
<td></td>
</tr>
<tr>
<td>Vascular puncture</td>
<td>5 (6.7)</td>
<td>2 (2.7)</td>
<td>0.442</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>0 (0.0)</td>
<td>1 (1.3)</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

Continuous variables are presented as mean ± SD; categorical variables are presented as count (percentage). Ordinal variables (number of passes and block-related pain) are presented as median [range].

Total anesthesia-related time is defined as the sum of performance and onset times. Onset and total anesthesia-related times are calculated only for patients with a minimal composite score of 14 points at 30 minutes.

CI indicates Confidence interval.
block. All $P$ values presented were 2-sided and values inferior to 0.05 were considered significant.

RESULTS

The 150 subjects were recruited during a period of 3.5 months (August 2015 to mid-November 2015) (Fig. 1). Sixty-seven, 60, and 23 patients were enrolled in Montreal, Chiang Mai, and Bangkok, respectively. A higher male-to-female ratio was present in the IV group. However, there were no intergroup differences in terms of age, body mass index, and American Society of Anesthesiologists physical status (Table 1). Technical execution (performance time/number of needle passes/procedural pain/complications) was comparable between the 2 groups (Table 2).

No intergroup differences were recorded in terms of onset time, success rate, and surgical anesthesia (Table 2; Fig. 2). However, compared with its IV counterpart, PN dexamethasone provided 19% to 22% longer durations for motor block ($15.7 \pm 6.2$ vs $12.9 \pm 5.5$ hours; $P = 0.009$), sensory block ($16.8 \pm 4.4$ vs $13.9 \pm 5.4$ hours; $P = 0.002$), and postoperative analgesia ($22.1 \pm 8.5$ vs $18.6 \pm 6.7$ hours; $P = 0.014$) (Table 2; Figs. 3–5).

Patient follow-up at 1 week revealed no sensory or motor deficit.

DISCUSSION

In this randomized trial, we compared IV and PN dexamethasone for US-guided ICB. Our results show that both modalities result in similar onset times and success rates. However, PN dexamethasone provides longer motor block, sensory block, and postoperative analgesia. Our findings echo those of Kawanishi et al.\textsuperscript{4} who observed a longer time to first analgesic request ($P = 0.008$) with PN compared to IV dexamethasone for interscalene blocks (with ropivacaine 0.75%). However, our trial contradicts past studies that reported similar block durations for the 2 modalities.\textsuperscript{15,18,23} We hypothesize that this discrepancy can be explained by differences in nerve block and LA. Alternately, similarities between IV and PN dexamethasone may stem from insufficient statistical power. For instance, in their trial on sciatic

![FIGURE 2. Percentage of patients with a minimal composite score of 14 points according to time. Absolute count values are provided inside each column. Dex, Dexamethasone.](image)

![FIGURE 3. Kaplan–Meier survival plot for the duration of motor block. $P = 0.020$ (log-rank test). Dex, Dexamethasone.](image)
blocks, Rahangdale et al.\(^\text{23}\) observed that PN dexamethasone prolonged motor block and time to first analgesia by 5 and 6 hours, respectively, but these values failed to reach statistical significance. For interscalene blocks, Desmet et al.\(^\text{18}\) recorded a longer analgesic duration with PN compared to IV dexamethasone (1405 vs 1275 minutes). Again the intergroup difference was not statistically significant. Finally, dose constitutes another confounding variable. In our trial, 5 mg was selected because recent studies suggest PN equivalency between small (4–5 mg) and large (8–10 mg) doses of dexamethasone.\(^\text{24}\) However, one cannot rule out the possibility that high doses could selectively increase block duration in the IV group thereby achieving parity with the PN route. For instance, Abdallah et al.,\(^\text{15}\) Desmet et al.,\(^\text{18}\) and Rahangdale et al.\(^\text{23}\) all used doses ≥8 mg. In fact, Abdallah et al.\(^\text{15}\) even observed that, with 8 mg, IV dexamethasone prolonged motor blockade to a greater extent than its PN counterpart. Thus, future dose-finding studies are required to elucidate the optimal dose of IV (and PN) dexamethasone.

Although statistically significant, the increased durations in sensorimotor block (2.8–2.9 hours) and postoperative analgesia (3.5 hours) may not seem clinically relevant. Admittedly, a 2.8-hour-longer motor block falls below the 3.3-hour threshold used in the sample size justification. However, the increased length of postoperative analgesia did cross the mark. More importantly, the longer block duration carries few additional risks because the ICB technique and dose of dexamethasone remain identical in both study groups. Thus, the cost–benefit ratio may favor the PN modality.

The lack of a control group requires discussion. In our study, all patients received either IV or PN dexamethasone. We decided to forego enrollment of a purely placebo group (IV and PN normal saline). We reasoned that, although the optimal method of administration remains controversial, the literature is replete with trials demonstrating that patients receiving dexamethasone fare better than those who do not in terms of onset time, block duration, postoperative analgesia, or opioid consumption.\(^\text{1–3,5–17}\) Furthermore, because our standard of practice includes dexamethasone (IV or PN), we felt that its non-inclusion would be unethical.

The fact that we only used patients with 14-point minimal composite scores to tabulate block duration also deserves special mention. In our trial, 87% to 88% of subjects reached 14 points (or more) at 30 minutes. In contrast, 95% to 99% of patients achieved surgical anesthesia. In theory, one could have a sensory block with minimal motor blockade and still display surgical anesthesia. Because our primary outcome was motor block duration, we erred on the side of caution and retained only

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**FIGURE 4.** Kaplan–Meier survival plot for the duration of sensory block. \(P = 0.012\) (log-rank test). Dex, Dexamethasone.

**FIGURE 5.** Kaplan–Meier survival plot for the duration of analgesia. \(P = 0.048\) (log-rank test). Dex, Dexamethasone.
subjects with minimal composite scores of 14 points. In a similar effort to maximize precision, we discarded patients whose blocks wore off during their sleep.

Our protocol contains some limitations. First, the durations of sensorimotor block and postoperative analgesia axiomatically depend on patient recall. Therefore, to minimize subjectivity, we selected motor block as the primary outcome and circumvented adverse effects. Because our trial was carried out in 3 centers and 2 countries, we feared that different patterns of opioid prescription might have constituted a confounding variable. Finally, although no neural deficit was observed in the PN group at 7 days, further studies are needed to validate the safety of PN dexamethasone.

In conclusion, compared with its IV counterpart, PN dexamethasone (5 mg) provides longer motor block, sensory block, and postoperative analgesia for US-guided ICB. Future dose-finding studies are required to elucidate the optimal dose of IV and PN dexamethasone.

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REFERENCES


