Dexamethasone Provides Longer Analgesia than Tramadol when Added to Lidocaine after Ultrasound Guided Supraclavicular Brachial Plexus Block. A Randomized, Controlled, Double Blinded Study

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Abstract

Background and aim: Tramadol and dexamethasone were proposed as adjuvants in regional anesthesia but there were no studies comparing those two molecules in ultrasound guided (US) peripheral nerve blocks. The aim of this controlled, randomized, double-blind study was to evaluate the effect of tramadol and dexamethasone added to lidocaine for a US guided supraclavicular brachial plexus (SCBP) block on duration of postoperative analgesia.

Methods: 60 patients undergoing upper extremity surgery. Exclusion criteria: history of lung disease, obesity (body mass index>30 kg/m2), chronic pain or psychiatric disorder, drug or alcohol abuse, and hypersensitivity to local anesthetics. The US-guided SBPB was performed with 2% lidocaine 15 mL plus either dexamethasone 8 mg (2 mL; dexamethasone Group) or tramadol 100 mg (2 mL; tramadol Group) or normal saline 2 mL (Saline Group). The following data were recorded for 24 hr after surgery: onset times and durations of sensory and motor block and duration of analgesia.

Results: Time for first analgesia demand was longer in the dexamethasone group than in tramadol group (P=0.001). The onset sensory and motor blockade was similar in each group. The duration of sensory block was higher in both adjuvant groups (P<0.001) than saline group and longer in the dexamethasone group compared with the tramadol group (P=0.01). Motor block was prolonged in adjuvant group compared with saline group (p<0.001) but no differences were found between tramadol and dexamethasone group (p=0.74).

Conclusions: The addition of dexamethasone to lidocaine for SCBP block prolongs the duration of analgesia and reduces postoperative pain without excessive associated motor blockade compared to tramadol.

Introduction

During nerve blocks (which can control postoperative pain effectively), various drugs have been proposed in combination with local anesthetics (LA) to help reduce onset time and to prolong the duration of action and postoperative analgesia. Dexmedethomidine, Clonidine and Ketamine are commonly used [1-3] but they induce several side effects.

Tramadol and dexamethasone were proposed as safe adjuvants to LA but there were no studies comparing these two drugs in ultrasound guided (US) peripheral nerve blocks.

Methods

After local ethics committee approval (provided by Tunisian Military Hospital Ethics committee, Tunis, Tunisia (Chairperson Prof H. Haouala) on 25 August 2012), recording in the Australian New Zealand Clinical Trials Registry with an assigned number of ACTRN12612000921886 and written informed consent, patients undergoing upper limb (wrist/hand/elbow or distal arm) surgery were recruited to this controlled, randomized, double-blind study.

Inclusion criteria were age ≥ 18 and ≤ 80 years and American Society of Anesthesiologists (ASA) physical status classification I-III. Exclusion criteria were obesity (body mass index > 30 kg/m2), a history of lung disease, chronic pain or psychiatric disorder, drug or alcohol abuse, and hypersensitivity to LA.

Patients definitively involved in this study were allocated into three groups using sealed opaque envelopes to receive either 15 ml lidocaine 2% with 2 ml of dexamethasone (8 mg) (dexamethasone group) or 15 ml lidocaine 2% with 2 ml of tramadol (100 mg) (tramadol group) or 15 ml lidocaine 2% with 2 ml of isotonic saline chloride (control group).

All LA solutions were prepared by an anesthesiologist not involved in the performance of SCBP block, patient care, or data collection. No premedications were applied to the patients. An intravenous cannula was inserted into the controlateral arm with continuous infusion of crystalloid solution. The patients were routinely monitored with electrocardiogram (ECG), non-invasive blood pressure (NIBP) measurement, and pulse oximetry (SpO2) during procedures.

For the SCBP block, patients were placed in the supine position, heads turned in opposite direction of the anesthetized limbs. The arm to be blocked was placed in neutral position, along the body.

Under sterile conditions, the linear type probe (12 MHz) of the

Keywords

Tramadol; Dexamethasone; Ultrasound; Analgesia; Brachial plexus block

Trial Registration

Australian New Zealand Clinical Trials Registry identifier: ACTRN12612000921886.
ultrasound equipment (Logiq 7° GE Health care, USA) wrapped within a rubber sheet (Vygon, France) was placed on the supraclavicular fossa to locate the subclavicular artery and brachial plexus (BP) cluster. After cutaneous LA infiltration, a 50 mm 22 G insulated short needle (Echoplex D 50 mm, Vygon, France) was inserted toward the BP cluster (from the lateral to medial) in the long axis of the ultrasound waves. Once the needle tip reached the BP cluster on the ultrasound image, the anesthetic solution was injected and the procedure time was noted.

All nerve blocks were performed by a single experienced anesthesiologist blinded to group allocation. Surgery was conducted with patients awake, and a surgical tourniquet was used in all cases. Additive general anesthesia was at the discretion of the anesthesiologist and was based on sensory blockade at 30 minutes and the intended area of surgery (leading to exclude the patient).

Patients were checked for voice changes, Horner’s syndrome, dyspnea or chest discomfort then the surgery was allowed.

After the end of the SCBP block, an anesthesiologist blinded to the solution type evaluated sensory block as follows: every five minutes until 30 minutes. Each dermatome (Table 1) was evaluated using a pinprick using a three-point scale and compared with the controlateral arm as a reference: 0 = normal sensation; 1 = loss of sensation of pinprick (analgesia); and 2 = loss of sensation of touch (anesthesia).

The motor block was evaluated by Bromage modified scale at 10, 20 and at the end of the 30 minute period (Table 2).

The success of bloc was defined by a complete sensory and motor block allowing surgery.

The onset times of the sensory and motor blockades were defined as the time interval between the end of LA administration and normal sensation (sensory score = 0) and absent movement (Bromage modified scale = 0), respectively in nerve specific territory.

Duration of sensory block and motor blockade was defined as the time interval between the end of LA administration and normal sensation (sensory score = 0) and recovery of complete motor function (Bromage modified scale = 4), respectively.

The postoperative analgesia was assessed at 1, 3, 6, 12, and 24 h and the time between the end of LA administration and the first analgesic request was recorded as the duration of analgesia (the patient received, if Verbal Analog Scale VAS ≥ 30, IV paracetamol 1 g and 0.15 mg/Kg morphine sub-cutaneously).

Duration of postoperative analgesia and proportion of patients requiring analgesic supplementation for the first 24h were the primary outcome variables. Onsets of anesthesia, duration of sensory and motor block, were the secondary end points.

### Statistics

In a preliminary unpublished analysis, we have found that duration of analgesia produced by 15 ml of 0.5 % bupivacaine was 4.2 ± 2 hours. With an alpha error of 5% and power of 80%, and assuming a 50% increase in the analgesia duration, we estimated that 14 patients would be needed in each group. Therefore 60 patients were included (20 patients in each arm).

### Statistical analysis

We compared categorical data, between the groups, using Pearson’s Chi-2 test. Categorical data was described by count (percentages). We evaluated the data distribution using the Kolmogorov-Smirnov test. We used One-way analysis of variance for normally distributed continuous variables (Dunnett’s T3 test was used for post hoc pair wise analysis). We compared groups using Kruskall-Wallis test for non-normally distributed continuous variables (Pair wise comparison was performed by Mann-Whitney’s U test). Continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range, depending on the normality distribution of the data. First postoperative analgesia request was compared between groups by Kaplan-Meier survival analysis.
analysis and log-rank test. A p value of less than 0.05 was considered significant. All statistics were done using R v.2.15.1 (R Development Core Team 2012).

Results

The flowchart of patients consented and recruited is shown in Figure 1.

The data of 60 patients were analyzed. As summarized in Table 3, the three groups were not different regarding to age, sex, body weight, height, procedure time and duration of surgery.

The success rate of all nerve blocks was 100% in the three groups.

Table 3: Patients' characteristics, procedure time and surgical duration.

<table>
<thead>
<tr>
<th></th>
<th>Saline Group (n = 20)</th>
<th>Tramadol Group (n = 20)</th>
<th>Dexamethasone Group (n = 20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>30 ± 8</td>
<td>31 ± 9</td>
<td>36 ± 10</td>
<td>0.12</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14 (70 %)</td>
<td>12 (60 %)</td>
<td>15 (75.0%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Female</td>
<td>6 (30 %)</td>
<td>8 (40 %)</td>
<td>5 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>74 ± 15</td>
<td>72 ± 10</td>
<td>78 ± 12</td>
<td>0.28</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173 ± 7</td>
<td>171 ± 6</td>
<td>174 ± 8</td>
<td>0.31</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>24.8 ± 4.2</td>
<td>24.7 ± 3.1</td>
<td>25.8 ± 3.6</td>
<td>0.56</td>
</tr>
<tr>
<td>Surgical duration (min)</td>
<td>85 ± 47</td>
<td>93 ± 36</td>
<td>113 ± 60</td>
<td>0.06</td>
</tr>
<tr>
<td>procedure time (sec)</td>
<td>240 (125; 280)</td>
<td>150 (140; 180)</td>
<td>240 (165; 300)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Table 4: Sensory and motor onset time (minutes).

<table>
<thead>
<tr>
<th></th>
<th>Saline Group (n = 20)</th>
<th>Tramadol Group (n = 20)</th>
<th>Dexamethasone Group (n = 20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial nerve (S)</td>
<td>10 (8 ; 12)</td>
<td>8 (8 ; 12)</td>
<td>12 (10 ; 15)</td>
<td>0.23</td>
</tr>
<tr>
<td>(M)</td>
<td>18 ± 8</td>
<td>20 ± 7</td>
<td>18 ± 5</td>
<td>0.71</td>
</tr>
<tr>
<td>Ulnar nerve (S)</td>
<td>10 (10 ; 12)</td>
<td>10 (6 ; 14)</td>
<td>12 (9 ; 13)</td>
<td>0.55</td>
</tr>
<tr>
<td>(M)</td>
<td>14 (14 ; 15)</td>
<td>22 (14 ; 24)</td>
<td>18 (15 ; 21)</td>
<td>0.13</td>
</tr>
<tr>
<td>Median nerve (S)</td>
<td>8 ± 3</td>
<td>8 ± 3</td>
<td>10 ± 4</td>
<td>0.29</td>
</tr>
<tr>
<td>(M)</td>
<td>10 (10 ; 12)</td>
<td>14 (10 ; 20)</td>
<td>15 (13 ; 18)</td>
<td>0.06</td>
</tr>
<tr>
<td>Musculocutaneous nerve (S)</td>
<td>6 (4 ; 8)</td>
<td>6 (6 ; 9)</td>
<td>10 (6 ; 11)</td>
<td>0.06</td>
</tr>
<tr>
<td>(M)</td>
<td>8 (5 ; 14)</td>
<td>11 (8 ; 15)</td>
<td>14 (12 ; 16)</td>
<td>0.31</td>
</tr>
<tr>
<td>Medial antebrachial cutaneous nerve (S)</td>
<td>8 ± 2</td>
<td>7 ± 2</td>
<td>9 ± 4</td>
<td>0.052</td>
</tr>
<tr>
<td>(M)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>

Categorical data was described by count (percentages); Continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range, depending on the normality distribution of the data.

S: sensory block; M: motor block; *: not applicable

Table 5: Duration of sensory and motor blocks.

<table>
<thead>
<tr>
<th></th>
<th>Saline Group (n = 20)</th>
<th>Tramadol group (n=20)</th>
<th>Dexamethasone Group (n = 20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radial nerve (S)</td>
<td>192 ± 47</td>
<td>256 ± 49 §</td>
<td>924 ± 84 §§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(M)</td>
<td>221 ± 63</td>
<td>309 ± 57 §</td>
<td>411 ± 109 §§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ulnar nerve (S)</td>
<td>198 ± 57</td>
<td>257 ± 36 §</td>
<td>955 ± 97 §§§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(M)</td>
<td>200(180; 210)</td>
<td>300(255; 350) §</td>
<td>423(353; 498) §§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median nerve (S)</td>
<td>172 ± 45</td>
<td>247 ± 51 §</td>
<td>916 ± 116 §§§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(M)</td>
<td>199 ± 54</td>
<td>279 ± 78 §</td>
<td>357 ± 139 §§§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Musculocutaneous nerve (S)</td>
<td>149 ± 42</td>
<td>228 ± 45 §</td>
<td>882 ± 121 §§§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(M)</td>
<td>182 ± 49</td>
<td>255 ± 54 §</td>
<td>288 ± 107 §§§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medial antebrachial cutaneous nerve (S)</td>
<td>151 ± 43</td>
<td>219 ± 44 §</td>
<td>849 ± 109 §§§</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>(M)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>

Categorical data was described by count (percentages); continuous variables were expressed as mean and standard deviation (SD) or median and interquartile range, depending on the normality distribution of the data.

S: sensory block; M: motor Block; *: not applicable

§: Significance between control group and adjuvant groups
‡: Significance between tramadol group and dexamethasone group

As shown in Table 4, the onset sensory and motor blockade was similar in each group. The duration of sensory block was higher in both adjuvant groups (p<0.001) than saline group and longer in the dexamethasone group compared with the tramadol group (P=0.01). Motor block was prolonged in adjuvant group compared with saline group (p<0.001) but no differences was found between tramadol and dexamethasone group (p=0.74) (Table 5).

Fewer patients required analgesia for 24 h in dexamethasone group versus tramadol group versus saline group (p<0.001). Patients in tramadol group required less first 24 h analgesia than saline group (p=0.04) (Table 6).

Time for first analgesia demand was longer in the dexamethasone...
group versus tramadol group (p<0.001) versus saline group (p<0.001) (Figure 2).

From the sixth hour, patients who received dexamethasone showed a significantly lower VAS than the other groups. On the other hand, patients of tramadol group showed significantly lower VAS than saline group (Figure 3).

Discussion

In this controlled, randomized, double-blinded study comparing dexamethasone versus tramadol as adjuvant to LA in US guided SCBP block, we found that 8 mg dexamethasone and 100 mg tramadol prolonged sensory and motor block and lengthen postoperative analgesia when associated with lidocaine 2%. In addition, onset of both blockade were not delayed with this two molecules in comparison to control group. Additionally, dexamethasone had a shorter motor blockade than tramadol and a very wide delayed time for first analgesia demand.

In a comparative study between tramadol and dexamethasone as associated to bupivacaine in SCBP block under nerve stimulation, Shrestha et al. [4], showed that the mean duration of postoperative analgesia in dexamethasone group was higher than in tramadol group (1028 ± 194.51 minutes vs. 453.17 ± 72.81 minutes; respectively). However, in our study, mean duration of analgesia in dexamethasone group were 1110 minutes and 240 minutes in tramadol group. Despite we used lidocaine; we found results that approximate those of Shrestha et al. [4]. The use of ultrasound guidance (injection too close to the nerves) and bupivacaine (long duration action) can explain the results.

In addition, they found that the sensory block onset was longer in tramadol group than in dexamethasone group (18.47 ± 2.03 minutes vs. 16.76 ± 2.34 minutes, respectively). Furthermore, there was no difference in motor block onset between groups (12.9 ± 1.49 minutes vs. 13.43 ± 1.66 minutes). These findings seem to be strange because sensory block was late compared to motor block.

Several studies showed that both tramadol [5-7] and dexamethasone [8-16], when added to peripheral nerve block, extend the duration and to improve the quality of postoperative analgesia.

Robaux et al. [5] found that tramadol added to mepivacaine 1.5% in axillary block did not neither increase the onset time of anesthesia (10 ± 4 minutes versus 18 ± 15 minutes; 100 mg tramadol and control group respectively) nor prolonged the duration of both blocks but prolonged the duration of postoperative analgesia in only tramadol 200 mg group.

Kaabachi et al. [6] reported that 100 mg tramadol (which was not associated with a delayed onset of anesthesia compared to control group) prolonged sensory and motor blockade after axillary block with lidocaine 1.5% with epinephrine 1/200,000 (190 ± 87 minutes and 180 ± 96 minutes respectively) but those results were shorter than we found (207 ± 37 minutes and 253 ± 54 minutes respectively). In addition, Kaabachi et al. [6] showed a prolonged postoperative analgesia with a longer time for first rescue analgesia in the only tramadol high dose group (200 mg) and fewer patients required analgesia for 24 h in both tramadol groups compared with the control group (26 (76%) and 31 (94%) respectively). This results was similar to us (16 (80%) and 20 (100%) respectively).

Kapral et al. [7] found no difference in onset of sensory and motor blockade if tramadol added to 40 mL of mepivacaine 1% in axillary plexus block but that the duration of both blocks was significantly longer. The duration of sensory and motor block in tramadol group was approximately similar (299 ± 84 and 259 ± 76 min) to our (207 ± 37 and 253 ± 54 minutes).

With the intention explaining the mechanism of action, Kapral et al. [7] demonstrates that IV tramadol has no effect on mepivacaine 1%
administered for axillary plexus block. They stipulated that probable mechanisms of action of tramadol as adjuncts to LA anesthetics for peripheral nerve block are essentially a local effect on the nerve and not vasoconstrictive effects.

The mechanism of the analgesia induced by steroids is not clear. Previous works [17,18] demonstrated that it is suspected to be mediated by their anti-inflammatory effects. Stan et al. [19] stipulated that the steroids suppress the synthesis of various inflammatory mediators, which prolongs the period of analgesia up to 48 hours. Attardi et al. [20] showed that dexamethasone acts on nociceptive C-fibers via glucocorticoid receptors increasing the inhibitory potassium channels activity. In our study, dexamethasone produced a relatively rapid effect which cannot be explained by the traditional theory of steroid action (nuclear transcription).

Another action mechanism of corticosteroids had been discussed. They may have a direct local effect on the nerve [21] but not categorically confirmed. However, there is little known about the functional or structural influence of steroids on normal peripheral nerve fibers [22].

Another possibility is that prolongation of LA block occurs because of systemic effects of dexamethasone. Some authors believe that analgesic properties of steroids are the result of their systemic effect [23,24].

We think that the most likely mechanism of analgesia induced by corticosteroids in SCBP block is its epidermal migration and therefore direct local effect. Many recent studies [25-27] showed that steroids, when injected (association with LA) epideral space, are an effective therapy for patients with disc herniation or radiculitis. So, another investigation with a control group receiving parenteral administration of dexamethasone is being conducting in our institution to confirm that theory.

Conclusion

To conclude, we can say that dexamethasone appears to be more powerful than tramadol with a dissociative effect on sensory nerve fiber which can be a patient satisfaction source. Further studies are needed to determine the optimal dose of dexamethasone to associate with LA to prolong nerve blocks as well as the mechanism of this effect.

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References


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