Efficacy of dexmedetomidine with ropivacaine in supraclavicular brachial plexus block for upper limb surgeries

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Abstract

Background and Aims: The primary aim of this study was to evaluate the effect of addition of dexmedetomidine on the duration of analgesia in patients undergoing upper limb surgeries under supraclavicular brachial plexus block.

Material and Methods: Sixty patients of American Society of Anesthesiologists physical status I/II/III undergoing elective upper limb surgeries under supraclavicular brachial plexus block using nerve stimulator were randomized into two groups. Group A (n = 30) received 30 mL 0.5% ropivacaine and 1 mL normal saline, and Group B (n = 30) received 30 mL 0.5% ropivacaine and 1 µg/kg of dexmedetomidine. The primary outcome was the duration of analgesia. Secondary outcomes included time to onset and duration of sensory/motor blockade.

Statistical Analysis: Results on continuous measurements are presented as mean ± standard deviation and compared using Student's unpaired t-test. Results on categorical measurements are presented in number (%) and compared using Chi-square test.

Results: Onset of sensory and motor block in Group A (13.0 ± 4.1 and 23.5 ± 5.6 min) was slower than those in Group B (9.5 ± 5.8 and 15.6 ± 6.3 min; P = 0.009 for sensory and P < 0.001 for the motor block). Duration of sensory and motor block in Group A (400.8 ± 86.6 and 346.9 ± 76.9 min) was shorter than those in Group B (630.6 ± 208.2 and 545.9 ± 224.0 min; (P < 0.001). The duration of analgesia in Group A (411.0 ± 91.2 min) was shorter than that in Group B (805.7 ± 205.9 min; P < 0.001). The incidence of bradycardia and hypotension was higher in Group B than in Group A (P < 0.001).

Conclusion: Perineural dexmedetomidine with ropivacaine provides prolonged postoperative analgesia, hastens the onset of sensory and motor block and prolongs the duration of the supraclavicular brachial plexus block.

Key words: Brachial plexus block, dexmedetomidine, regional anesthesia, ropivacaine

Introduction

Peripheral nerve blockade is an integral part of comprehensive anesthetic care. Regional anesthesia techniques provide important advantages including excellent pain control, reduced side-effects, and shortened stay in the post anesthesia care unit. However, these early advantages can be short-lived and limited by the relatively brief duration of action of currently available local anesthetics (LAs), potentially resulting in block resolution before the period of worst postoperative pain. Increasing the volume of LA may prolong the duration of analgesia, but may also increase the risk of LA systemic toxicity. Although continuous catheter-based nerve blocks can extend postoperative analgesia, their placement requires additional time, cost, and skill.

Ropivacaine has a long duration of action, with similar pharmacology to bupivacaine but a wider safety margin.¹⁻⁵ Adjuvants with LAs in brachial plexus block are used to achieve a quick, dense, and prolonged block.⁶⁻⁹
The concurrent injection of α2 adrenergic agonist drugs has been suggested to improve the nerve block characteristic of LA solutions.\textsuperscript{[10]} Dexmedetomidine is a selective α2 adrenoceptor agonist, which has higher affinity to α2 receptors compared to clonidine. With ropivacaine, it results in a dose-dependent increase in the duration of sensory and motor block.\textsuperscript{[6,7,10-14]}

However, their combination in supraclavicular brachial plexus block has not been studied till now; hence, the need for the study.

The primary outcome was the duration of analgesia. Secondary outcomes include the time to onset of sensory and motor blockade, duration of sensory and motor block and was supplemented with general anesthesia.

Material and Methods

This placebo-controlled randomized trial was conducted at a tertiary referral hospital from October 2012 to April 2014. Sample size calculation was done based on a pilot study in which it was estimated that a minimum of ten patients in each group would be required to detect a difference in the average duration of analgesia as small as 2 times with 95% confidence level. The standard deviation (SD) of the two groups was 80 and 137 min of A and B Groups, respectively. The level of significance and the power of the study were fixed as 0.05 (α) and 0.9 (1-β). A larger sample size of 30 in each group was selected to avoid the skewness of the primary outcome variable (time to first analgesic), to obtain significant difference in the secondary outcomes among the two groups and to eliminate any other confounding biases.

Eligible participants were patients aged between 18 and 70 years, American Society of Anesthesiologists physical status (ASA) I/II/III, and those undergoing elective upper limb surgeries. Exclusion criteria were patient refusal for the block, patients on anticoagulants or with bleeding disorders, those with severe respiratory disease, neurological deficits involving the brachial plexus, allergy to study drugs, local infection at the injection site, those on sedatives or antipsychotics, body mass index (BMI) > 35, cardiac arrhythmias, advanced heart block and/or severe ventricular dysfunction, those on other vasodilators or negative chronotropic agents, altered sensorium, and pregnant and nursing women.

Sixty patients satisfying the inclusion criteria undergoing elective upper limb surgery were included in the study, after obtaining an informed consent and ethical committee approval. They were randomized and divided into two groups in a double-blind fashion using computer generated random number table with assignments provided in sealed opaque envelopes. Group A patients (n = 30) received 30 mL of 0.5% ropivacaine + 1 mL saline, and Group B patients (n = 30) received 30 mL of 0.5% ropivacaine + 1 µg/kg dexmedetomidine.

All the patients were premedicated with 150 mg ranitidine and 8 mg ondansetron orally on the morning of surgery. Intravenous access was obtained on the opposite limb. After documenting the baseline vital parameters, the patients received intravenous midazolam 1 mg and fentanyl 0.5 µg/kg prior to the block. The supraclavicular brachial plexus block was performed by the classical approach using a single-injection and nerve stimulator technique. Once the desired response was obtained, that is a muscle twitch of the fingers that is clearly visible; the current strength was reduced to 0.6 mA. If the desired response persisted at 0.6 mA, the drug solution was injected. If there was no adequate response, the needle was moved anteriorly or posteriorly along the first rib to elicit a response. Following the injection, the area was massaged to help the solution to dissipate along the plexus.

Sensory block was assessed by pinprick test at each minute after completion of drug injection in the dermatomal areas corresponding to the median nerve, ulnar nerve, radial nerve, and musculocutaneous nerve till complete blockade. Sensory block was assessed by a 3 - point scale: 0 - normal sensation, 1 - loss of sensation of pinprick (analgesia), 2 - loss of sensation of touch (anesthesia). Onset time was defined as the time interval between the end of LA administration and complete sensory block (score 2). Duration of sensory block was defined as the time interval between the end of LA administration and the complete resolution of anesthesia (score 0).

Motor blockade was assessed by modified Bromage scale (MBS) for the upper limb.\textsuperscript{[7,15]} Motor block onset time was defined as the time interval between the end of total LA administration and complete motor block (MBS score 2). Duration of motor block was defined as the time interval from the onset to the recovery of complete motor function (MBS score 0).

Inadequate sensory and motor blockade beyond 30 min following the infiltration was considered as an unsuccessful block and was supplemented with general anesthesia.

Pain was assessed using a standard 10 cm visual analog scale (VAS) by an independent anesthesiologist. Intraoperative heart rate, systolic, diastolic and mean arterial pressures, sensory and motor block scores, and the VAS scores were noted every 5 min during the first 15 min, then every 15 min throughout the surgery and hourly thereafter till complete recovery of the block. Intravenous paracetamol 1 g was...
administered 6th hourly for the first 24 h. Time for the first request of postoperative analgesic when VAS >3 (duration of analgesia) was noted and rescue analgesic intramuscular tramadol, 50 mg was given.

Hypotension (systolic blood pressure more than 20% fall from baseline value), bradycardia (heart rate <50/min), and postoperative complications such as nausea and vomiting, Horner’s syndrome, phrenic nerve palsy, pneumothorax, respiratory depression, and signs and symptoms of LA systemic toxicity were looked for and managed, if any. The above assessments were made by an investigator who was blinded to the drugs used in the study.

**Statistical analysis**

Results of continuous measurements were presented as mean ± SD and analyzed using Student’s unpaired t-test.

Results of categorical measurements were presented in number (%) and compared using $\chi^2$ test of significance. In the above tests, a $P < 0.05$ was accepted as indicating statistical significance. Data analysis was carried out using Statistical Package for Social Science Version 18 (SPSS Inc., Chicago, IL, USA) and Microsoft word and Excel were used to generate graphs and tables.

**Results**

A total of eighty patients were approached for participation in the study from October 2012 to April 2014. Fourteen patients did not satisfy the inclusion criteria. Sixty six patients were recruited and randomly assigned to their treatment group. Six patients were excluded after randomization due to patchy block. Finally, data from sixty patients were analyzed [Figure 1].

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**Figure 1:** Patient flow (according to consort chart)
There was no significant difference in the patient characteristics including age, gender, height, weight, BMI, ASA grade, type of surgery, and duration of surgery as summarized in Table 1.

Onset of sensory and motor blockade was significantly faster in Group B compared to Group A [Table 2]. Duration of analgesia and duration of sensory and motor blockade were also prolonged in Group B compared to Group A [Table 2].

The hemodynamic variables were comparable between the two groups during the study intervals except that intraoperatively four patients in dexmedetomidine group developed hypotension (13%), which was managed with a fluid bolus, and one patient had bradycardia (3%), which was managed by awakening the patient. There was statistically significant difference between the two groups in the incidence of these side effects (P < 0.001). There were no other side effects such as nausea and vomiting, Horner’s syndrome, phrenic nerve palsy, pneumothorax, or respiratory depression in any of the patients.

Discussion

Our study demonstrated that addition of an alpha agonist like dexmedetomidine to ropivacaine resulted in prolonged duration of analgesia postoperatively. It also showed that there were early onset and prolonged duration of sensory and motor blocks. By increasing the duration of analgesia with a single block, we could achieve a longer duration of postoperative analgesia without significant clinical side-effects.

Esmatoglu et al. added dexmedetomidine to levobupivacaine for axillary brachial plexus block and showed that it shortens the onset time of both sensory and motor block (9.0 ± 1.1 and 9.5 ± 1.0 min vs. 10.5 ± 1.3 and 11.1 ± 1.2 min, respectively), prolongs the duration of block (887 ± 66.2 and 773.0 ± 67.6 min vs. 673.0 ± 73.8 and 575.0 ± 65.0 min, respectively), and the duration of postoperative analgesia (1008.7 ± 164.0 vs. 887.1 ± 260.8 min, respectively), which is similar to our study.[14]

Addition of dexmedetomidine to bupivacaine during infraclavicular brachial plexus block under ultrasound guidance was studied where there was early onset of sensory and motor blockade, with prolonged analgesia and prolonged duration of sensory and motor block similar to our study.[16]

In another study, adding dexmedetomidine to ropivacaine for posterior tibial nerve block under ultrasound guidance had prolonged duration of sensory blockade (21.5 vs. 16.2 h); mean pairwise difference 5.3 h similar to the present study but with higher incidence of hypotension and bradycardia.[17]

Addition of dexmedetomidine to bupivacaine for greater palatine nerve block has demonstrated that increased duration of analgesia (22 ± 1.7 h) can be achieved, which is identical to that in our study.[13]

Brummett et al. showed that dexmedetomidine enhances duration of bupivacaine anesthesia and analgesia when used for sciatic nerve block in rats without any damage to the nerve.[18]

In another study, perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolonged the duration of analgesia by blocking the hyperpolarization-activated cation, which was reversed by a hyperpolarization-activated cation channel enhancer but not by α2 adrenoceptor antagonist. This indicates that the analgesic effect of peripheral perineural dexmedetomidine was caused by the enhancement of the hyperpolarization-activated cation current, which maintains the nerve in a hyperpolarized state and prevents it from subsequent firing.[19]

The efficacy of peripheral action of perineural dexmedetomidine added to bupivacaine and ropivacaine for sciatic nerve block in rats has been established. The increase in duration of analgesia is dose dependent, and the effect is peripheral (not caused by centrally mediated or systemic analgesia).[19,20]

In our study, the higher incidence of bradycardia and hypotension in dexmedetomidine group is a problem

Table 1: Comparison of demographic variables

| Parameters                  | Group A (n=30) | Group B (n=30) | P     |
|-----------------------------|---------------|---------------|-------|
| Age (years)                 | 40.6±15.2     | 41±15.5       | 0.933 |
| Gender: Male/female         | 20/10         | 20/10         | 1.000 |
| Weight (kg)                 | 62.1±8.9      | 64.9±11.3     | 0.296 |
| Height (m)                  | 1.6±0.1       | 1.6±0.1       | 0.240 |
| BMI (kg/m²)                 | 23.3±3.25     | 23.7±4.0      | 0.629 |
| ASA: Grade (I/II/III)       | 15/2/13       | 15/5/10       | 0.432 |
| Type of surgery: Orthopaedic/vascular/plastic | 14/11/5 | 14/9/7 | 0.766 |
| Duration of surgery (min)   | 100.3±39.35   | 91.0±38       | 0.354 |

Values are expressed as the mean±SD or the number of patients.
Group A = Ropivacaine + saline group, Group B = Ropivacaine + dexmedetomidine group, ASA = American Society of Anesthesiologists, SD = Standard deviation, BMI = Body mass index

Table 2: Block onset and duration between groups

| Time                        | Group A (n=30) | Group B (n=30) | P     |
|-----------------------------|---------------|---------------|-------|
| Onset of sensory block (min)| 13.0±4.1      | 9.5±5.8       | 0.009 |
| Onset of motor block (min)  | 23.5±5.6      | 15.6±6.3      | <0.001|
| Duration of sensory block (min) | 400.8±86.6 | 630.6±208.2   | <0.001|
| Duration of motor block (min) | 346.9±76.9   | 545.9±224.0   | <0.001|
| Mean duration of analgesia (min) | 411.0±91.2 | 805.7±205.9   | <0.001|

Values are expressed as the mean±SD.
Group A = Ropivacaine + saline group, Group B = Ropivacaine + dexmedetomidine group, SD = Standard deviation
and cannot be ignored. There was no significant clinical impact, and they could be easily managed. Bradycardia and hypotension are potentially life-threatening, and if not detected in time, there can be dangerous consequences. Thus, when dexmedetomidine is being used as an adjuvant to ropivacaine, monitoring of the patient in a high dependency area is required at least for 24 h.

The lack of other side effects such as nausea, vomiting, and respiratory depression make dexmedetomidine an attractive choice as an adjuvant for the block.

Use of ultrasound guidance for the peripheral nerve block is one of the latest, precise, and safe methods these days. This could have helped us to reduce the dosages and volumes of LAs. Long-term follow-up of our patients was not done. This could have helped us to understand any long-term neural side effects of the study drugs used. Nonavailability of ultrasound equipment during the course of our study and no long-term follow-up are our limitations. Further studies using ultrasound guidance and with long-term follow-up may be needed.

The findings of this study indicate that dexmedetomidine can be safely used with LA in peripheral nerve blocks; however, study to determine any toxic effects on neural structures in humans is needed.

Conclusions

We conclude that dexmedetomidine added to perineural ropivacaine in supraclavicular brachial plexus block is effective in providing prolonged duration of analgesia.

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Conflicts of interest

There are no conflicts of interest.

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