American Journal of Medical Case Reports, 2016, Vol. 4, No. 10, 336-338
Available online at http://pubs.sciepub.com/ajmcr/4/10/2

DOI:10.12691/ajmcr-4-10-2

Ultra-low Dose Naloxone Added to 0.5% Bupivacaine Significantly Prolongs the Duration of Analgesia Following Supraclavicular Brachial Plexus Block

Amal A M Al-Shukaili[1,*], Khoula M S AL-Mandhari[1], Basman Younis[1], Shobha Lad[1], Awadh Othman[1], Sachin Jose[2]

[1]Department of Anesthesia & ICU, Khoula Hospital, Muscat, Sultanate of Oman
[2]Oman Medical Specialty Board, Muscat, Sultanate of Oman
*Corresponding author: drnareshkaul@gmail.com

Abstract In this prospective, randomized, double-blind study, we evaluated the effect of ultra-low dose of naloxone on duration of supraclavicular brachial plexus block. It was hypothesized that naloxone can prolong the duration of sensory block. Following approval by Hospital Ethical Issues Committee, eighty patients scheduled for upper limb surgery under supraclavicular brachial plexus block were randomly allocated into control group who received 20ml bupivacaine with 3 ml normal saline (Group B) or study group that received 20ml bupivacaine with 100 mcg. of naloxone in 3 ml saline, (Group BN). Onsets of sensory and motor blockade were assessed at an interval of 3 min following the block. Duration of sensory and motor block was considered to be the time interval between the complete block and the first post operative pain reported by patient and complete recovery of motor functions respectively. The difference in onset time for sensory and motor block was statistically significant between two groups but clinically it may be considered insignificant. The recovery of sensory block was slower in group BN (15.6 ± 3.2 hr) compared to group B (13.3 ± 2.4 hr) [p=0.0001]. The recovery of motor block was slower in group B (13.3 ± 2.5 hr) compared to group BN (11.6 ± 4.3) [P=0.03]. In conclusion, addition of ultra-low dose of naloxone to bupivacaine in supraclavicular block prolongs the duration of sensory block and reduces duration of motor block significantly as compared to bupivacaine alone.

Keywords: *supraclavicular block, naloxone, bupivacaine, ultrasound guidance*

Cite This Article: Amal A M Al-Shukaili, Khoula M S AL-Mandhari, Basman Younis, Shobha Lad, Awadh Othman, and Sachin Jose, "Ultra-low Dose Naloxone Added to 0.5% Bupivacaine Significantly Prolongs the Duration of Analgesia Following Supraclavicular Brachial Plexus Block." *American Journal of Medical Case Reports*, vol. 4, no. 10 (2016): 336-338. doi: 10.12691/ajmcr-4-10-2.

1. Introduction

Ultrasound guided supraclavicular brachial plexus block provides a reliable regional technique for upper extremity surgery. [1,2] Various additives have been used for prolonging the regional block. [3,4].

Ultra-low dose of naloxone have been shown to release endorphins and also displace endorphins from receptor site. [5] Animal experiments have shown the safety of intrathecal naloxone administration. [6,7]

In this prospective, randomized, double-blind study, we evaluated the effect of an ultra-low dose of naloxone added to bupivacaine on the duration of sensory and motor block for post-operative analgesia following supraclavicular brachial plexus block. Wehypothesized that naloxone will prolong the duration of sensory block when added to bupivacaine during supraclavicular brachial plexus block. Our primary outcome was the onset and duration of sensory block, whereassecondary outcome was onset and duration of motor block.

2. Methods

After obtaining approval from the hospital ethical issues committee and informed verbal consent, eighty patients with American society of Anesthesiologist (ASA) physical status I-III, between age 20 and 80 years undergoing elective surgery for hand, forearm or elbow with duration of one to two hour were selected and included in this prospective, randomized, double blind study that was done at our tertiary care hospital (Khoula Hospital, Sultanate of Oman), over two years. Patient who gave a history of allergy to naloxone or bupivacaine, had coagulopathy or hepatic/ renal failure, local infection at the puncture site or systemic infection, pre-existing neuropathy of the limb to be operated, chronic obstructive pulmonary disease or respiratory failure and/or pregnancy were excluded from the study. Our patients were randomly allocated into two groups comprising forty patients in each using computer based randomization technique:

Group B, control group (n=40) received bupivacaine 0.5% 20 ml and 3 ml isotonic saline.

Group BN, study group (n=40) received bupivacaine 0.5% 20ml mixed with naloxone 100ng in 3 ml saline. The total volume was 23ml in either group. All patients received 1 mg midazolam iv prior to the procedure to reduce anxiety. The study medications were prepared by an anesthesiologist as per group randomization and thereafter the same anesthesiologist administered the block.

In the induction room, standard monitoring was initiated that included electrocardiography, pulse oximetry, and noninvasive blood pressure. Thereafter, intravenous fluid was started. The designated anesthesiologist proceeded to perform the supraclavicular block under ultrasound guidance. After performing the block, the onset of sensory block was checked by pinprick method, with 22 G hypodermic needle at an interval every 3 min to a maximum of 30 minutes in the sensory distribution of radial, ulnar, median and musculocutaneous nerves. The motor block was assessed by modified Lovettrating scale (6-normal muscular force, 0-complete paralysis). [8]

The sensory and motor block onset time was defined as the time between the end of the local anesthetic injection and complete absence of pinprick response in all nerve distribution and complete paralysis (Lovett rating scale =0) respectively.

For duration of sensory block, we recorded the time interval between complete sensory block & the first postoperative pain reported by the patient. Duration of motor block was recordedas the time interval between complete paralysis & complete recovery of motor function as per Lovett rating scale from 0 to 6.Cases with a failed supra-clavicular block were to be excluded from the study and administered general anesthesia and a new patient inducted. An investigator who was not aware of the patient group recorded all data.

3. Sample Size Estimation

The sample size of forty patients in each group was estimated to give the study power of >80% for a significant difference at p<0.05.

4. Statistical Analysis

Data have been presented in the tables as mean ± Standard deviation (mean± SD),or frequencies (number of cases). Comparison of numerical variables between the two groups was done using students t test for independent samples. We used Chi square test for comparing categorical data. All statistical calculations were done using computer program Statistical Package for the Social Science (SPSS) under the guidance of a statistician.

5. Results

Demographic data including age, weight, and patient gender were comparable in both groups (Table 1).

Table 1. Demographic data in the two groups

Demographic Parameter	Group B (n= 40)	Group BN (n= 40)	p value
Age in yr			
20-39	35 (87.5%)	28 (70.0%)	0.18
40-59	5 (12.0%)	10 (25.0)	
≥60	0	2 (5.0)	
Gender			
Male	34 (85.0%)	30 (75.0%)	0.4
Female	6 (15.0%)	10 (25.0%)	
Weight in kg			
30-59	13 (32.5%)	19 (47.5%)	0.115
60-89	24 (60.0%)	21 (52.5%)	
≥ 90	3 (7.5%)	0	

Statistical test: Chi-square.
n= number of patients.

The block characteristics are shown in Table 2.The onset time for sensory block was significantly (p=0.008) shorter in group BN (16.0± 5.2 min)as compared to group B (19.3±5.4min) statistically, but clinically it may not be significant as the difference was only two minutes. The onset time of motor block was longer in group B (25.5±7.0 min) as compared to group BN (21.9±7.6 min). Again, this statistically significant difference (p=0.03) may be considered clinically insignificant.

Table 2. The block characteristic between two groups

Parameter	Group B(n=40) (Mean ±SD)	Group BN(n=40) (Mean ±SD)	p-value
Onset sensory(min)	19.28±5.44	16.00±5.24	0.008
Onset motor(min)	25.53±7.03	21.90±7.57	0.029
Duration of sensory block (hr)	13.28±2.39	15.65±3.15	0.0001
Duration of motor block (hr)	13.30±2.49	11.55±4.27	0.029
Surgery duration(min)	87.3±41.73	71.88±36.61	0.082

Statistically significant (p<0.05),
Statistical Test: independent sample t-test.

The difference in the duration of surgery was not significant between the two groups (p= 0.08).

The recovery of sensory block was significantly longer in group BN(15.6±3.2 hr) compared to group B (13.3±2.4 hr) [p=0.0001]. In contrast, the recovery of motor block was longer in group B (13.3±2.5) compared to group BN (11.6±4.3) with a p value of 0.03. All of these were analyzed using independent sample t-test where p<0.05 was considered significant.

6. Discussion

The finding of the present study showed that addition of an ultra-low dose (100 mcg) of naloxone to 20ml 0.5% bupivacaine without any opioid for supraclavicular brachial plexus block can significantly increase the duration of sensory block, a difference of three hours. In

addition, ultra low dose naloxone reduced the duration of motor blockade by approximately two hours. We also noted a statistically significant difference in the sensory and motor block onset time but this may not be considered significant clinically.

In this study the requirements for postoperative analgesia were not significantly different between two groups. A larger sample size would probably be necessary to observe a clinically significant difference between groups if it at all exists.

A previous study has demonstrated that the addition of a low dose of naloxone to lidocaine 1.5% with or without fentanyl in axillary brachial plexus block, increased the time for the first patient request of additional postoperative analgesics and duration of motor block. [4] This finding is in agreement to that observed in the present study where we too noted a prolongation of sensory block.

In another study, it has been demonstrated that addition of low-dose naloxone to 0.5% bupivacaine, with or without fentanyl in supraclavicular brachial plexus block, prolongs the duration of both sensory and motor block. [9] However our study showed that 100ng naloxone shortens the duration of motor block, which is in contrast to the findings of Marashi et al (2015). [9] This difference may be attributed to their use of a larger volume of bupivacaine (30 ml) as well as a small sample size of 17 patients in each group.

Evidence suggests that naloxone produces a dose dependent pain response in both animals and human. In rat model, small doses of naloxone produced paradoxical analgesia, whereas larger doses resulted in hyperalgesia. [10,11] An ultra-low dose of naloxone can augment the anti-nociceptive effect of morphine by enhancing the reuptake of excitatory amino acids from the synaptic cleft. [12] In our study, we observed that ultra-low dose of naloxone can enhance the bupivacaine effect even without opioid.

Naloxone in low doses is known to release endorphins or displace endorphins from receptor sites. [5] This may explain the reason for a sensory block prolongation by naloxone. This phenomenon may elucidate the naloxone-induced sensory block prolongation in patients of our study.

Two studies were published in addition to this study that evaluated a low dose of naloxone as adjuvant to local anesthetic. [4,9] Both these studies had used similar dose of naloxone (100 mcg). However a larger sample size with variations in the dose of naloxone is needed in future to determine the optimal dose of naloxone for prolongation of sensory bock.

In this study, to eliminate all possible confounding factors, the anesthesiologist who prepared drugs and administered the block was different from anesthesiologist who collected the data.

In conclusion, the addition of ultra-low dose of naloxone to 0.5%bupivacaine solution without opioid in supraclavicular brachial plexus block was noted to prolong the duration of sensory block and reduce the duration of motor block. Further studies are needed to evaluate and determine the optimal doses needed for prolongation of peripheral nerve sensory block, as well as to further explore the exact mechanism of naloxone for prolonging the peripheral nerve block.

References

[1] Kapral S, Krafft P, Eibenberger K,Fitzgerald R, Gosch M, Weinstabl C. Ultrasound-guided supraclavicular approach for regional anesthesia of the brachial plexus. Anesth Analg 1994; 78: 507-513.

[2] Williams SR, Chouinard P, Arcand G, Harris P, Ruel M, Boudreault D, et al. Ultrasound guidance speeds execution and improves the quality of supraclavicular block. Anesth Analg 2003; 97: 1518-1523.

[3] Movafegh A, Razazian M, Hajimohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. Anesth Analg 2006; 102: 263-267.

[4] Ali M, Behrang N, Mustafa S, Omid N. An ultra-low dose of Naloxone added to lidocaine or lidocaine-fentanyl mixture prolongs axillary brachial plexus blockade. Anesth Analg 2009;109:1679-1683.

[5] Gan TJ,Ginsberg B, Glass PS, Fortney J, Jhaveri R, Perno R. Opioid-sparing effect of a low-dose infusion of naloxone in patient-administered morphine sulfate Anesthesiology 1997; 87: 1075-1081.

[6] Cole DJ, Drummond JC, Shapiro HM, Hertzog RE, Brauer FS.The effect of fentanyl anesthesia and intrathecal naloxone on neurologic outcome following spinal cord injury in the rat. Anesthesiology 1989; 71:426-430.

[7] Sinz EH, Kofke WA, German RH. Phenytoin, midazolam and naloxone protect against fentanyl induced brain damage in rats. Anesth Analg 2000; 91:1443-1449.

[8] Acalovschi I, Cristea T. Intravenous regional anesthesia with meperidine. Anesth Analg 1995;81:539-543.

[9] Marashi SM, Sharifnia HR, Azimaraghi O, Aghajani Y, Barzin G, Movafegh A. Naloxone added to bupivacaine or bupivacaine-fentanyl prolongs motor and sensory block during supraclavicular brachial plexus blockade. ActaAnaesthScand 2015; 59: 921-7.

[10] Levine JD,Gordon NC. Method of administration determines the effect of naloxone. Brain Res 1986;365:377-378.

[11] Levine JD,Gordon NC, Fields HL. Naloxone dose dependently produces analgesia and hyperalgesia in postoperative pain. Nature 1979;278:740-741.

[12] Tsai RY,Tai YH, Tzeng JI,Lin SL, Shen CH, Yang CP,et al. Ultra-low dose naloxone restores the anti-nociceptive effect of morphine in pertussis toxin-treated rats and prevents glutamate transporter down-regulation by suppressing the p38 mitogen-activated protein kinase signaling pathway. Neuroscience 2009;159:1244-1256.