Buprenorphine Improves the Efficacy of Bupivacaine in Nerve Plexus Block: A Double Blind Randomized Evaluation in Subclavian Perivascular Brachial Block

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Citation

A Jadon, M Panigrahi, S Parida, S Chakraborty, P Agrawal, A Panda. *Buprenorphine Improves the Efficacy of Bupivacaine in Nerve Plexus Block: A Double Blind Randomized Evaluation in Subclavian Perivascular Brachial Block*. The Internet Journal of Anesthesiology. 2007 Volume 16 Number 2.

Abstract

Background: Studies examining the benefit of adding analgesic to brachial plexus block have produced mixed results. Although the mechanism of action of these analgesics remains unclear, buprenorphine have been used successfully in brachial block for prolonged postoperative pain relief. We compared the onset, quality and duration of analgesia produced by bupivacaine, either alone or combined with buprenorphine.

Material & Methods: A prospective, randomized double blind study was conducted. Forty patients scheduled to undergo surgery for upper limb under Supraclavicular subclavian perivascular brachial plexus block (SSPB) were included to evaluate the effect of Buprenorphine when mixed with 0.3% bupivacaine used for brachial plexus block. Group-I (control group) (n=20) patients received 30 ml 0.3% bupivacaine+ 1 ml saline and intramuscular 1ml drug(3 gkg 1 buprenorphine + saline to make volume= 1 ml). Group-II (study group) (n=20) patients received 30 ml 0.3% bupivacaine+ 1 ml study drug (3 gkg 1 bupivacaine + saline to make volume= 1 ml) and 1 ml of intramuscular injection of saline.

Results: In Group-I the onset time for motor block was 4.05±0.944 min. and sensory block was 6.65± 1.182 min. Group-II the onset time for motor block was 3.75±1.208 min. and sensory block was 4.25±1.25 min. This difference was not significant (p<0.404) for sensory and (p<0.152) for motor block. The mean duration of satisfactory analgesia was 331.2± 33.54 minutes in Group-I and 680.6±86.27 minutes in Group-II the difference in duration between two groups was significant (p<0.0001). The mean duration of motor block was not significant, 309±26.1 minutes in Group-I and 329± 28.4 minutes in Group-II (p<0.352).

Conclusion: We conclude that the addition 3 gkg 1 buprenorphine to 0.3% bupivacaine mixture for perivascular brachial block in upper limb orthopedic surgery increase the time for complete sensory block. It improves the quality of block and lengthens the duration of analgesia without affecting the duration of motor block.

INTRODUCTION

To date, results of studies evaluating the efficacy of opioids and local anesthetic combinations in the brachial plexus are inconclusive [1,2,3,4]. However, over the past 20 years, several studies have suggested that the addition of certain opiates to the local anesthetic used for brachial block may provide effective, long-lasting postoperative analgesia [3,4]. Some studies indicated that the agonist-antagonist, buprenorphine, added to bupivacaine provided a longer period of postoperative analgesia than the traditional opiates. This practice can be of particular benefit to patients undergoing ambulatory upper extremity surgery by providing prolonged analgesia after discharge from the hospital. [5,6,7,8] We conducted a prospective double blind study to evaluate the effect of mixing buprenorphine with bupivacaine used for perivascular brachial plexus block. The observations were made for the effect of buprenorphine on the onset of block, quality and duration of postoperative analgesia and associated side effects.

PATIENTS AND METHODS

After approval of the ethical committee, forty healthy consenting adult patients scheduled for upper extremity surgery were enrolled in the study. Premedication was

provided by tab. Alprazolam 0.5 mg orally 1 hr. before surgery. Anesthesia was given by a subclavian perivascular brachial plexus block. Patients were assigned randomly to either of two groups based on the agents used for the blocks. Group-I (control group) (n=20) patients received 30 ml 0.3% bupivacaine+ 1 ml saline and intramuscular 1ml drug(3 µgkg $^{-1}$ buprenorphine + saline to make volume= 1 ml). Group-II (study group) (n=20) patients received 30 ml 0.3% bupivacaine+ 1 ml study drug (3 µgkg $^{-1}$ bupivacaine + saline to make volume= 1 ml) and 1 ml of intramuscular injection of saline. The study was kept double-blind by having 1 anesthesiologist prepare the solutions, a second anesthesiologist performs the blocks, and third anesthesiologists monitor the anesthesia and analgesia thereafter, up to and including the time of the first request for an analgesic medication. The data were reported as means (+/- SD), and differences between groups were determined using repeated measures of analysis of variance (ANOVA) and followed by T test for comparison by using 'AcaStat' statistical computer software, P value of < 0.05 was considered to be statistically significant.

Technique: After sterile preparation of the region the 22G, 4 cm needle was inserted through the skin wheel and above the palpating finger immediately lateral to the subclavian artery. Needle was directed 45 degree dorso-laterally parallel to the scalene muscles and toward the elbow of the patient. There was a click once the sheath pierced and entered. The patient felt paresthesias of the hand and fingers once the tip of the needle crossed the perineural sheath. Drug was injected after repeated aspiration to avoid inadvertent vascular entry. After injection, the sensory block tested by sensations to pin prick. Motor block was evaluated by thumb movements e.g. abduction (Radial nerve), adduction (Ulnar Nerve), opposition (Median nerve). Musculocutaneous nerve block assessed by flexion of elbow and supination-pronation of forearm. Hollmen scale was used to assess both sensory and motor blockade. The eight nerves were evaluated for sensory function and four nerves studied for motor blockade. Evaluation was carried out for every minute after completion of the injection and the time of onset was noted for both sensory and motor blockade. Onset of block was defined as minimum of grade 2 in Hollmen scale. Block was considered complete when sensory and motor scores were grade 3 in Hollmen scale. Duration of sensory blockade was considered as the time interval between the local anaesthetic injection and the onset of pain in the postoperative period. The duration of motor blockade was considered as the time interval between injection of local anaesthetic and recovery of muscle power. When separate nerve blocks or supplementation with IV analgesia or general anaesthesia was required due to inadequate/ failed block were not included in study. Intra-operative and postoperative complications were recorded. All patients were monitored with continuous Pulse, ECG, SpO2 and NIBP every 5 minutes intra-operatively and continuous SpO2 and one hourly Pulse and NIBP post-operatively. Postoperative analgesia was provided by Injection Diclophenac sodium 75 mg IM on demand. Injection Ondansetron 4 mg IV was given for PONV.

HOLLMEN SCALE

Sensory Block : 1 = normal sensation of pinprick, 2 = pin prick felt as sharp pointed but weaker compared with same area in the other upper limb, 3 = pin prick recognized as touch with blunt object, 4 = no perception of pin prick.

Motor block : 1= normal muscle function, 2 = slight weakness in function, 3= very weak muscular action, 4 = complete loss of muscle action.

OBSERVATIONS

Figure 1

Table 1: Demographic profile

	Group-I	Group-II	p value
Age Yr. (Mean ± SD)	30.5 (11.2)	28.2 (10.58)	p <0.508*
Weight Kg (Mean ± SD)	52.36 (8.38)	55.85(10.29)	p <0.301*
Sex M : F	16:4	17:3	

p*= not significant

Figure 2

Table 2: Type of Surgery

Nature of Surgery	Number of patients (n)	
	Group-I	Group-II
Open reduction & Internal Fixation (ORIF) Both Bones	12	15
Open reduction & internal fixation (ORIF) Single Bone	4	2
Tendon transfer	2	1
Bone Biopsy	0	1
Removal of Implants	2	1
Total duration Min. (Mean± SD)	144 ± 36*	136 ± 45*

P* <0.1695 (not significant)

Table 3: Comparison between Group-I, and Group-II for onset time, time taken for complete block, duration of sensory and motor block

Figure 3

Time in Minutes (Mean ± SD)	Group-I	Group-II	p value
Onset Time for Motor Block	4.05 (0.944)	3.75 (1.20)	p <0.152
Onset Time for Sensory Block	6.65 (1.182)	4.25 (1.25)	p <0.404
Time to Complete Motor Block	17.05 (2.633)	19.2 (3.53)	p <0.105
Time to Complete Sensory Block	20.5 (2.50)	22.4 (3.80)	p <0.037*
Duration of Motor Block	300.9 (26.01)	329.2 (28.4)	p <0.352
Duration of Sensory Block	331.2 (33.54)	680.6 (86.27)	p <0.0001*

* Statistically Significant

Figure 4

Table 4: Intensity of Block (Hollmen's Scale):

	Grading	Group-I	Group-II	
Sensory	1	0	0	P<0.05**
	2	3	1	
	3	10	5	
	4	7	14	
Motor	1	0	0	
	2	3	1	P<0.322*
	3	11	9	
	4	6	10	

*Not Significant

** Significant

Figure 5

Table 5: Complications and Side effects

Complications	Group-I	Group-II	Measures Taken
Arterial puncture	1	1	Needle repositioned,
Nausea and Vomiting	2	2	Inj. Ondansetron 4mg IV given
Inadequate Block	2*	1* 1**	* Inj. Ketamine **Separate ulner nerve block given
Failed Block	1	0	General Anaesthesia given
Horner's Syndrome	2	3	
Serious complications	Nil	Nil	

No statistical significant difference among Groups.

RESULTS

In Group-I the onset time for motor block was 4.05±0.944 min. and sensory block was 6.65± 1.182 min. Group-II the onset time for motor block was 3.75±1.208 min. and sensory block was 4.25±1.25 min. This difference was not significant (p<0.404) for sensory and (p<0.152) for motor block. There was no significant deference in to achieve complete motor block 17.05± 2.633 min. in Group-I and, 19.2± 3.53 min. in Group-II (p<0.105). The complete sensory block took significantly longer time in Group-I 22.4± 3.8 min. than Group-II 20.5±2.5 min. (p<0.037).

The mean duration of satisfactory analgesia was 331.2± 33.54 minutes in Group-I and 680.6±86.27 minutes in Group-II the difference in duration between two groups was significant ($p<0.0001$). The mean duration of motor block was not significant, 300.9±26.1 minutes in Group-I and 329.2± 28.4 minutes in Group-II ($p<0.352$). Intensity of motor block (number of cases in different grade) were comparable ($P<0.322$), but there was significant difference in quality of sensory block ($P<0.05$).

Two patients had arterial puncture (one in each group), needle was repositioned and block was completed. Both the blocks were effective. Inadquate block occurred in 3 patients (one in Group-I and two in Group-II) required injection ketamine 25mg increments (50-100mg), one of such patient was given ulner block with 5 ml 0.25% bupivacaine posted for ORIF fracture both bone left forearm.Complete Failed block occurred in one patient of Group-I, conventional GA with relaxant was given due to required difficult surgical position (# both bones and olecranon ORIF through posterior approach). Nausea and vomiting occurred in 4 patients(two patients of each group) managed with one Intravenous dose of Injection Ondansetron 4 mg. Horner's syndrome was seen in 5 patients (2 in Group-I and 3 in Group-II) without any sequelae. No patient develop any serious complications due to block procedure (pneumothorax, large hematoma or prolonged nerve palsy) or buprenorphine (respiratory depression) etc. There was no signifant difference in complications between two Groups.

DISCUSSION

This prospective, randomized, double blind study was done in 40 patients scheduled for upper limb surgery under subclavian perivascular brachial block (Winnies' approach) [10] with similar surgical and demographical profile (Table 1& 2). We have used the Intramuscular buprenorphine in control group so that the systemic analgesic effect of buprenorphine can be differentiated from its peripheral action. [5,7]

Results of this study show that addition of 3 $\mu g kg^{-1}$ buprenorphine to 0.3% bupivacaine mixture for perivascular brachial block in upper limb orthopedic surgery improves the quality of sensory block and lengthens the duration of analgesia without affecting the duration of motor block.

Buprenorphine-local anesthetic perivascular brachial plexus block provided postoperative analgesia lasting 3 times longer than local anesthetic block alone and twice as long as buprenorphine given by IM injection plus only local anesthetic block have been reported. This supports the concept of peripherally mediated opioid analgesia by Buprenorphine. [5] The addition of buprenorphine to the local anesthetic used for brachial plexus block in the present study provided a 2-fold increase in the duration of postoperative analgesia, with complete analgesia persisting 5-7 hours beyond the duration provided by the local anesthetic alone in most of the patients. This practice can be of particular benefit to patients undergoing ambulatory upper extremity surgery by providing prolonged analgesia after discharge from the hospital [7] . In our study the mean duration of satisfactory analgesia with buprenorphine was 680.6 minutes is simillar as reported in other studies (14-34 hrs.). [5,6,7]

Ortells Polo et al [11] in their study of modified supraclavicular perivascular block recorded an onset time of 4.9+ 0.2 minutes and the time for motor paralysis at 15.2+ 6.9 minutes. This study support our data i.e. in Group-I the onset time for motor block was 4.05±0.944 min. and sensory block was 6.65± 1.182 min. Group-II the onset time for motor block was 3.75±1.208 min. and sensory block was 4.25±1.25 min.

In our study, we noticed that buprenorphine does not affect the onset of sensory or motor block; rather the complete sensory effect was delayed significantly than control group. Nishikawa K et al have shown that addition of fentanyl to lidocaine causes an improved success rate of sensory blockade but a delayed onset of analgesia due to decreased pH of the mixture. [12] In our study the onset of motor block was significantly faster than sensory block in both the groups (Group-I and Group-II), this can be explained by ‘core and mantle' concept of Winnie et al, 1977. [13]

Opioids have long been thought to act exclusively within the central nervous system. An increasing number of studies recently reported the existence of opioid receptors outside the central nervous system and therefore suggested that opioids are also able to produce analgesic effects in the periphery. [14] Experimental studies have shown that opioids could produce two types of effect on neuronal excitability. The first one is a local anesthetic action on the nerve fiber with a diminution of sodium and potassium conductance. The second is due to a linkage of the opioid with a receptor on the internal face of the membrane. Opioids could also migrate to the posterior horn of the spinal cord after linkage with axonal receptors. These findings expand the gate control theory of pain and suggest new approaches such as the development of peripherally acting opioid analgesics

without central side-effects. [15] No serious complications related to block technique or addition of buprenorphine were observed in present study (Table 5).

Clinical studies have proved that opioid injection in the brachial plexus produce a prolonged analgesia in the postoperative period. The more liposoluble opioids like fentanyl and buprenorphine are the more effective [16]. Our study and other studies [5,6,7,8] have shown that addition of buprenorphine to local anaesthetic increase the postoperative analgesia to a great extent, however the controversy still exist. Trials of a higher quality are needed to provide a definitive answer. [17]

CONCLUSION

We conclude that the addition 3 μgkg $^{-1}$ buprenorphine to 0.3% bupivacaine mixture for perivascular brachial block in upper limb orthopedic surgery does not effect the onset time for motor as well as sensory block. It delays in completion of sensory effect. It improves the quality of sensory block and lengthens the duration of analgesia without affecting the duration of motor block.

References

1. Bouaziz H, Kinirons BP. Sufentanil does not prolong the duration of analgesia in a
mepivacaine brachial plexus block: a dose response study. Anesth Analg. 2000
Feb;90(2):383-7.
2. Fletcher D, Kuhlman G, Samii K. Addition of fentanyl to 1.5% lidocaine does not

increase the success of axillary plexus block. Reg Anesth 1994;19:183- 8.
3. Bourke DL, Furman WR. Improved postoperative analgesia with morphine added to

axillary block solution. J Clin Anesth. 1993 Mar-Apr;5(2):114-7.
4. Flory N, Van-Gessel E, Donald F, Hoffmeyer P, Gamulin Z Does the addition of

morphine to brachial plexus block improve analgesia after shoulder surgery? Br J

Anaesth. 1995 Jul;75(1):23-6.
5. Candido KD, Winnie AP, Ghaleb AH, Fattouh MW, Franco CD Buprenorphine added

to the local anesthetic for axillary brachial plexus block prolongs postoperative

analgesia. Reg Anesth Pain Med. 2002 Mar-Apr;27(2):162-7.
6. Bazin JE, Massoni C, Bruelle P, et al. The addition of opioids to local anaesthetics in
brachial plexus block: the comparative effects of morphine, buprenorphine and
sufentanil. Anaesthesia 1997;52:858-62
7. Candido KD, Franco CD, Khan MA, Winnie AP, Raja DS. Buprenorphine added to
the local anesthetic for brachial plexus block to provide postoperative analgesia in
outpatients. Reg Anesth Pain Med 2001 Jul-Aug; 26(4):352-6.
8. Viel EJ, Eledjam JJ, De La Coussaye J, D'Athis F. Brachial plexus block with opioids

for postoperative pain relief: comparison between buprenorphine and morphine. Reg

Anesth 1989;14:274-8
9. G Caponga, D celleno et al. Alkalization of local anesthetics. Which block, which

anesthetics? Reg. Anesth 1995 Sept-Oct;20(5): 369-77.
10. Quang Hieu De Tran et al Brachial Plexus Block: a review of techniques. Can J

Anesth.2007;54(8):662-674.
11. Winnie AP, Collins VJ. The subclavian perivascular technique of brachial plexus

anaesthesia. Anaesthesiology 1964;25:353.
12. Nishikawa K, Kanaya N, Nakayama M, Igarashi M, Tsunoda K, Namiki A. Fentanyl

improves analgesia but prolongs the onset of axillary brachial plexus block by

peripheral mechanism. Anesth Analg. 2000 Aug; 91(2):384-7.
.
13. Winnie AP, Tay CH, Patel KP, Ramamurthy S et al. Pharmacokinetics of local

anaesthetics during plexus block. Anesth Analg 1977;56:852-861.
14. Stein C, Hassan AH. Local analgesic effect of endogenous opioid peptides.

Lancet 1993 Aug 7; 342:321-4.
15. Janson W, Stein C. Peripheral opioid analgesia. Curr Pharm Biotechnol. 2003

Aug; 4 (4):270-4.
16. Boogaerts J, Lafont N. Mechanism of action and clinical use of opioids administered

by the peripheral perineural route Can Anesthesiol. 1991;39(2):91-5
17. PR Picard, MR Tramer, HJ McQuay and RA Moore. Analgesic efficacy of

peripheral opioids (all except intra-articular): A qualitative systematic review of

randomised controlled trials. Pain. 1997; 72:309-31

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