

Original Article

Buprenorphine as an Adjuvant to Bupivacaine in Supraclavicular Brachial Plexus Block

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Abstract

Background and aims : Adjuvants used in peripheral nerve blocks prolong duration of analgesia without prolonging motor blockade or causing systemic side effects. The current study was conducted to evaluate the efficacy of buprenorphine as an adjuvant to bupivacaine in supraclavicular brachial plexus block.

Methodology : A prospective randomised double blind study was conducted on 50 adult patients between 20- 60 years, weighing > 60 kgs, belonging to American Society of Anaesthesiology class I and II, scheduled to undergo elective upper limb orthopaedic procedures. Patients were randomised into 2 groups of 25 each. Patients in group A (n=25) received supraclavicular brachial plexus block with 25 ml 0.5% bupivacaine and group B (n=25) patients received supraclavicular brachial plexus block with 25 ml 0.5% bupivacaine and 3 mcg/ kg of buprenorphine. Onset of sensory and motor blockade, duration of analgesia and postoperative VAS scores were noted.

Results : Duration of analgesia was significantly longer in group B (13.24 hrs) compared to group A (6.68 hrs), with a p value <0.000. No statistical difference was found in the mean onset time of sensory and motor blockade, postoperative VAS scores or postoperative morphine consumption. No side effects were noted.

Conclusion : Addition of buprenorphine 3 mcg/ kg as an adjuvant to 0.5% bupivacaine in supraclavicular brachial plexus block prolongs postoperative analgesia without causing systemic side effects.

Key Words: Adjuvants, Buprenorphine, Supraclavicular brachial plexus block, Analgesia

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Introduction

Peripheral nerve blocks provide ideal operating conditions during surgery by reducing stress response, with minimal interference to physiological functions of the body. General anaesthesia requires polypharmacy, whereas peripheral nerve blocks, with minimal drugs provide excellent intraoperative and post operative analgesia preserving an alert, awake and cooperative patient. The problem solely with local anaesthetics is that they cannot provide prolonged postoperative analgesia. Several adjuvants have been tried with local anaesthetics to prolong the duration of postoperative analgesia without prolonging motor blockade or causing systemic side effects. The demonstration that opioid receptors are present in the peripheral nervous system by Fields et al¹ in 1980 prompted recent investigations on the use of opioids either alone or combined with local anaesthetics for regional anaesthesia procedures like brachial plexus block. Important factors determining the duration of action include lipid solubility and the affinity of different opioids for their receptors. Opioids like morphine, tramadol, buprenorphine etc. are used as adjuvants. Several studies have shown that the addition of buprenorphine, an agonist antagonist opioid to bupivacaine^{2,3,4,5} produces longer postoperative analgesia compared to other opioids. The aim of this

randomized double blind prospective study was to clinically evaluate the efficacy of buprenorphine as an adjuvant to bupivacaine in a dose of 3 mcg/kg body weight for supraclavicular brachial plexus block in patients undergoing upper limb orthopaedic procedures with regards to the onset and duration of both sensory and motor blockade.

Materials and methods

After obtaining institutional ethics committee approval and written informed consent, 50 adult patients in the age group of 20-60 years, weighing > 60kg, without any neurological deficit and local sepsis, belonging to ASA I & II scheduled to undergo elective upper limb orthopaedic procedures were chosen. All the patients were assessed and those with normal clinical, biochemical, hematological and radiological parameters were selected. Patient with history of allergy to local anaesthetics and those with cardiovascular and respiratory disorders, and extremely obese patients with difficult landmarks were excluded from the study. Informed written consent was obtained from all the patients. All the patients were randomly allocated into group A or group B using a computer generated random table. Group A (n=25) : patients undergoing supraclavicular brachial plexus block by

subclavian perivascular technique with 25 ml of 0.5% bupivacaine. Group B (n=25) : patients undergoing supraclavicular brachial plexus block by subclavian perivascular technique with 25 ml of 0.5% bupivacaine and 3mcg/kg of buprenorphine.

On arrival of the patient in the operating room pulse oximetry, non invasive blood pressure and electrocardiogram were connected and baseline values of heart rate, blood pressure, respiratory rate and oxygen saturation were recorded. An intravenous access was obtained in the opposite arm. According to group allocation, the test solution was prepared by an anaesthetist who did not participate further in the study. The patients were given supraclavicular brachial plexus block by the subclavian perivascular technique under aseptic precautions using nerve stimulator guidance. 25ml of the test solution, either 0.5% bupivacaine alone or 0.5% bupivacaine with 3 mcg/kg buprenorphine was injected after careful negative aspiration.

Non invasive blood pressure and heart rate were measured every minute for the first 10 minutes and every 5 minutes thereafter throughout the intra operative period. Heart rate and rhythm by electrocardiogram and oxygen saturation by pulse oximetry were monitored continuously. They were documented at 1, 2, 5, 10, 15, 30 minutes and every 30 minutes thereafter. Following the administration of the drug patients were evaluated every minute till the onset of sensory and motor blockade. Time of onset of sensory blockade was tested by the time in minutes from the injection of the drug to the lack of appreciation of pin prick sensation at C5 dermatome with a 26G hollow needle. Onset of motor blockade was assessed by the time in minutes from the time of drug injection to the loss of shoulder abduction. Failure of the block to appear in 20 minutes was taken as failure and the patients were administered general anaesthesia and were excluded from the study. After confirmation that the block has taken up, surgery was started. During the surgical procedure, the degree of pain was assessed with a 3 point verbal rating score. The verbal rating score utilizes objectives to describe the intensity of pain such as no pain, pain and unbearable pain and was scored as 0 = no pain, 1 = mild pain, 2 = unbearable pain. If verbal rating score was > 1, patients were administered general anaesthesia to complete the surgery and were excluded from the study. Local anaesthetic toxic reactions including subjective and objective manifestations like circumoral numbness, tinnitus, twitching, convulsions, etc., were looked for and appropriate measures were planned. Complications associated with the technique like intravascular injection, intrathecal injection, epidural injection and pneumothorax were looked for and appropriate measures were planned. Duration of analgesia was tested post operatively using the visual analogue score (0-10) every 1/2 hour for the first 6 hours thereafter every 2 hours till 24 hours thereafter every 3 hours till 48 hours. Patients were given rescue analgesia with intravenous morphine 3 mg when VAS \geq 4 upto a maximum of 30 mgs in 24 hrs. Side effects of opioids like nausea and vomiting, pruritus, urinary retention, hypotension, headache, respiratory depression defined as respiratory rate < 10/minute and

any other neurological depression were monitored for 48 hours.

Duration of analgesia is the time in hours from the onset of analgesia to the time of administration of rescue analgesia. Side effects of buprenorphine were monitored for a period of 48 hours from the time of administration of the drug.

The parameters of age, weight and duration of surgery were analysed using the ANOVA test. The sex distribution in the two groups were analysed with the Pearson's Chi - Square test. Onset time for motor and sensory blockade were analysed using the ANOVA test. Duration of analgesia in the two groups was analysed with the t-test and the statistical significance estimated. A p value of < 0.05 was considered statistically significant.

Observations and Results

The patients included in this study were divided into two groups consisting of 25 patients each.

Group A (n=25) received 0.5% bupivacaine

Group B (n=25) received 0.5% bupivacaine + 3mcg/kg of buprenorphine.

Table 1- Demographic parameters

PARAMETERS	GROUP A N = 25	GROUP B N = 25
Mean Age in years (S.D)	37 (1.44)	37 (1.44)
Sex ratio Male: Female	20:5	20:5
Mean Weight in kg (S.D)	63.5 (1.44)	63.5 (1.44)

Table 2- Type of surgical procedure and mean duration of surgery

Parameters	Group A	Group B
Type of surgery	ORIF-25	ORIF-25
Duration of surgery (mins)	127.60 \pm 6.64	128.60 \pm 7.14

ORIF – Open reduction and internal fixation

Table 3. Mean onset time of motor & sensory blockade

PARAMETERS	GROUP A N=25 (S.D)	GROUP B N=25 (S.D)
MOTOR BLOCKADE	3.18 (0.061)	3.25 (0.086)
SENSORY BLOCKADE	6.31 (0.080)	6.17 (0.081)

Table 4. Duration of Analgesia in Hours

Group	N	Mean (hours)	SD	p Value
A	25	6.68	0.082	<0.000
B	25	13.24	0.081	

There was no statistically significant difference in age, sex ratio or weight among the two groups (Table 1).

The two groups were well matched for the type of surgical procedure and duration of surgery, suggesting postoperative pain of similar intensity (table 2).

Onset of sensory and motor blockade in the two groups was comparable and there was no statistically significant difference among the two groups (Table 3).

Patients in group B had a longer duration of analgesia than patients in group A and the difference was statistically significant (Table 4).

There was no statistically significant difference in the vital signs like heart rate, systolic blood pressure, and diastolic blood pressure from the baseline throughout the surgery in the two groups. The groups did not show statistical difference in the postoperative VAS scores or postoperative morphine consumption. None of the patients in the two groups developed nausea, vomiting, pruritus, hypotension, respiratory depression or any other neurological depression.

Discussion

The subclavian perivascular approach to the brachial plexus has gained popularity because of the satisfactory anaesthesia and less failure rate with this approach. Franco CD, Vieira ZE⁶ in their study on subclavian perivascular brachial plexus block found that the subclavian perivascular block provides an effective block for the surgery on the upper extremity. They also concluded that at the site of injection with this technique the plexus is reduced to its smallest components and the sheath is reduced to its smallest volume, which explains in greater part the success obtained with this block. Lanz⁷ and his colleagues in their study on the extent of blockade following various techniques of brachial plexus block demonstrated that the subclavian perivascular approach to the brachial plexus resulted in a homogenous blockade of the nerves of the brachial plexus. With the interscalene approach to the brachial plexus, made at the level of the nerve roots, C8 and T1 are likely to be missed because of the vertical arrangement of the roots. Thus the interscalene approach tends to fail on the ulnar side of the limb in a dermatomal distribution. In contrast, the axillary approach is made at the level of the terminal nerves and the musculocutaneous and radial nerves are the most likely nerves to be inadequately blocked resulting in failure within a terminal nerve distribution.

With the supraclavicular technique these complications are not seen. There is a 0.6 - 25% incidence of pneumothorax, which is usually asymptomatic. With the interscalene approach, dangerous and potentially lethal complications like vertebral artery injection and subarachnoid or epidural injection can occur. Therefore, in this study the subclavian perivascular approach to the brachial plexus was used.

Cheryl et al⁸ in their comparative study of 0.25% bupivacaine and 0.25% ropivacaine for brachial plexus block demonstrated a higher incidence of required supplementation. Therefore, they recommend using 0.5% concentration of these local anaesthetics to provide brachial plexus anaesthesia. Therefore, in this

study 0.5% bupivacaine was used. However in a study by Gupta et al, ED 50 dose of bupivacaine was not dependent on concentration. The median effective volume for 0.25%, 0.375% and 0.5% bupivacaine for supraclavicular block was 26.8, 18.1 and 12.0 ml respectively. Lowering concentration led to increase in volume required for block. The block in this study was done under ultrasound guidance⁹. In our study, we used nerve stimulator guidance for giving the block. So a higher volume of drug was selected.

According to Franco CD, Vieira ZE⁶ in the subclavian perivascular technique the solution is delivered at a point in which the trunks are compactly arranged. So a volume of 20-30 ml of local anaesthetic solution is sufficient. Therefore, in this study a volume of 25 ml was used.

The demonstration of opioid receptors in the peripheral nervous system by Fields et al¹ in 1980 prompted recent investigations on the use of opioids either alone or combined with local anaesthetics for regional anaesthesia procedures like brachial plexus block. In this study, the efficacy of buprenorphine as an adjuvant to bupivacaine in brachial plexus block was evaluated. Buprenorphine in a dose of 3 mcg/kg is used in supraclavicular block, and is found to be effective^{10,11}. Even in a dose of 0.3 mg added to local anaesthetic in supraclavicular block, no adverse effects have been encountered^{12,13}. In our study, the mean weight of patients selected was 63.50+/-1.44Kgs and buprenorphine was used on a weight basis at 3mcg/kg with 25ml (0.5%) bupivacaine for subclavian perivascular brachial plexus blockade.

Onset of sensory and motor blockade : The onset of sensory analgesia was tested by loss of pinprick sensation in the C5 dermatome. In this study the mean onset of sensory analgesia was 6.31 minutes in group A and 6.17 minutes in group B. The difference was not statistically significant among the groups.

The onset of motor blockade was tested by loss of shoulder abduction. In this study the mean onset time for motor blockade was 3.18 minutes in group A and 3.25 minutes in group B. The onset time for motor blockade was thus similar in the two groups, the difference being statistically insignificant. The data and results reported by Ashok Jadon¹⁰ and his colleagues and Amol Singam et al¹² on the addition of buprenorphine to bupivacaine for brachial plexus block were similar to these findings and support these observations. In these studies also the onset of motor block was earlier than the onset of sensory block, which can be explained by the "core and mantle" concept by Winnie and Ramamoorthy¹⁴. However, in the study by Bharat Paliwal et al the onset of sensory blockade was 8.25+ 3.93 mins. 0.25% bupivacaine was used in their study, and the delay might be attributed to the difference in concentration of the local anaesthetic used. Also in their study, motor blockade followed sensory blockade¹³.

Duration of analgesia : In this study the mean duration of sensory blockade in group A was found to be 6.68 hours and 13.24 hours in group B. Thus the addition of buprenorphine 3 mcg/kg significantly prolongs the duration of analgesia.

In the study by Kenneth D. Candido¹⁵ and colleagues the addition of 0.3mg of buprenorphine conferred a mean duration of post operative analgesia of 22.3 hours compared to 6.6 hours with the local anesthetic alone. In another study¹⁶ by the same authors, the mean duration of post operative analgesia was found to be 5.3 hours with the local anaesthetic alone as compared with 17.4 hours when 0.3mg of buprenorphine was added. In both these studies a volume of 40 ml of local anaesthetic was used, and 0.3 mgs buprenorphine was used, both of which are higher than the volume and dosage used in our study. This might explain the longer duration of analgesia attained in their study compared to our study. In the study by Singam et al¹², addition of 0.3 mg buprenorphine to 38 ml of 0.25% bupivacaine produced significantly longer sensory blockade (647.83= 55.7 mins) compared to bupivacaine alone (322.16= 31.80 mins). Though a large volume of drug was used in this study, the concentration of drug used was less, which might explain similarity in the duration of sensory blockade with our study. In the study by Ashok Jadon¹⁰ and his colleagues the addition of 3mcg/Kg of buprenorphine as an adjuvant to 30ml of 0.3% bupivacaine for subclavian perivascular brachial plexus blockade conferred a mean duration of 680.6 +/-86.27 minutes as compared to 331.2 +/- 33.54 minutes with 30ml of 0.3% bupivacaine alone, similar to our study.

Side effects and Hemodynamic parameters : None of the patients in the two groups showed any of the side effects like nausea, vomiting, pruritus, urinary retention, hypotension, headache, sedation or respiratory depression. In the study performed by Kenneth D. Candido¹⁶ there was a 5% incidence of nausea, vomiting and pruritus when buprenorphine was added to the local anesthetic. In the study of 20 patients by J.E. Bazin et al¹⁷ 1 patient reported drowsiness, 4 patients reported pruritus, 6 patients had nausea and 4 patients had vomiting.

In this study there was no significant change in the hemodynamic parameters from the baseline in all the groups.

Conclusion

The addition of 3mcg/kg of buprenorphine to 0.5% bupivacaine in supraclavicular brachial plexus block provides a significant advantage over plain bupivacaine in terms of postoperative analgesia without any systemic side effects.

Conflict of Interest: Authors declare no conflict of interest.

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Pulse your way to healthy living!

Overweight and obesity are worldwide problems. Together, they affect more than a third of world's population. The need to keep the weight in check has spawned a whole lot of dietary regimens and novel exercises. Now in a new systematic review and meta-analysis (Siyong S. Li et al. Dietary pulses, satiety and food intake: A systematic review and meta-analysis of acute feeding trials. *Obesity*, 2014; 22 (8): 1773 DOI: 10.1002/oby.20782) published in the latest issue of *Obesity*, the authors claim that consumption of about 160 g of pulses (peas, lentils, beans, chickpeas) everyday might help to regulate your weight much better. The pulses are relatively rich in protein and have low glycaemic index. They can adequately replace animal protein and trans-fats in our regular diet. Besides pulses make people feel fuller with less quantities. The benefit is fairly uniform across all age groups and body mass indexes.

- Dr. K. Ramesh Rao

Red Hot Chilli Peppers Keep Your Bowel Healthy

If you are a chilli lover, you should rejoice! For your love may prevent colorectal cancer. Chilli peppers contain an active ingredient called Capsaicin. In a new experimental study carried out in University of California, San Diego (Petrus R. de Jong et al. Ion channel TRPV1-dependent activation of PTP1B suppresses EGFR-associated intestinal tumorigenesis. *Journal of Clinical Investigation*, 2014; DOI: 10.1172/JCI72340) the investigators administered capsaicin to mice genetically predisposed to develop colonic tumours. They found that capsaicin caused reduction in the tumour burden and prolonged the lifespan of the mice by 30%. This effect was potentiated by simultaneous administration of COX 2 inhibitors. Capsaicin activates a receptor/ion channel called TRPV1. TRPV1 has been called the molecular pain receptor. When it is activated it causes feedback inhibition of EGFR, thus acting as a tumour suppressor. So, chilli peppers don't just spice up your food, they spruce up your bowel too!

- Dr. K. Ramesh Rao