Original Research Article

Comparative clinical evaluation of buprenorphine versus morphine as adjuvant to bupivacaine in supraclavicular brachial plexus block for upper limb surgery

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Abstract

Background: The supraclavicular brachial plexus block with local anesthetics is one of the most commonly used regional nerve block technique for upper limb surgeries being to their high success rate and ability to provide prolonged postoperative pain relief. Opioid has been used as an adjuvant to prolong analgesia with local anesthetic. **Aim**: Aim of study to evaluate the quality and duration of postoperative analgesia by adding buprenorphine and morphine to local anesthetic solution. **Method**: A prospective, observational study was conducted on 60 healthy patients of ASA grade I and II of age group 18-45 years scheduled for upper limb surgery under supraclavicular brachical plexus block. Patients were allocated into two groups, 30 in each group. Group BB (buprenorphine group) received: 0.5% Bupivacaine 20 ml + 3µg/kg Buprenorphine + 10ml normal Saline. Group BM (morphine group) recieved: 0.5% Bupivacaine 20ml + 75 µg/kg Morphine + 10ml normal Saline. The parameters observed were onset and duration of sensory and motor block, quality and duration of analgesia and side-effects. **Result:** The mean duration of postoperative analgesia was significantly longer in group BB (20.6±2.11hrs) than in group BM (13.03±1.32hrs). There was no difference between two groups on mean onset of sensory and motor block. The mean duration of sensory block was significantly longer in group BB (539.67±13.22min) than in group BM (312±9.38min) with $p<0.05$. The mean duration of motor block was insignificant The mean duration of motor block was also significantly longer in group BB (310.67±15.42min) than in group BM (178±9.79min) with $p<0.05$. **Conclusion:** Addition of 3µg/kg buprenorphine to 0.5% buprenorphine for supraclavicular brachical plexus block prolonged duration of postoperative analgesia and sensory blockade than morphine without an increase in side effects.

Key words: Bupivacaine, buprenorphine, morphine, supraclavicular brachical plexus block.

Introduction

Regional anesthesia is one of the well-known anesthesia technique that has some additional benefits compared to general anesthesia[1,2]. Brachial plexus block is a popular peripheral nerve block technique providing ideal intraoperative anesthesia and analgesia for upper limb surgeries[3-5]. Since the introduction of brachial plexus block in clinical practice, many local anesthetics drugs had been used. However, large volume of local anesthetic required to produce desirable effects may result into systemic side effects[6,7].

Over many years a variety of adjuvant drugs like epinephrine, alpha2-agonist and opioids have been tried with local anesthetics in an attempt to provide prolong intraoperative anesthesia and analgesia[8].

Buprenorphine is highly lipophilic partial opioid receptor agonist with local anesthetic like properties to block voltage-gated sodium (Na+) channel, has a longer duration of action, commonly used adjuvant, easily available and cost effective[9,10].

We evaluated the hypothesis that addition of set equipotent doses of buprenorphine and morphine as an adjuvant to local anesthetic in brachial plexus block with supraclavicular brachical plexus bock enhances the postoperative analgesia.

The aim of our study was to evaluate and compare the onset, duration of action of sensory and motor blockade, postoperative analgesia with buprenorphine and morphine added to local anesthetic for supraclavicular brachial plexus block for upper limb surgeries.

Materials and Methods

After taking institutional ethics committee approval (35697-99/MC/IEC) and written informed consent from the patients, this prospective, observational study was conducted in Department of Anesthesiology and associated Hamidia hospital. Sixty patients scheduled for elective surgery of ASA grade I and II of either sex and age group between 18yrs-45yrs were included in study undergoing upper limb surgeries.Non-consenting patients, patients with contraindications to regional anaesthesia, neurological disease, spine/neurological deformities, local infection at site of injection, history of seizures, coagulopathy disorders, known allergy to local anesthetic solution and ASA grade III, IV, V were excluded from the study. After satisfying inclusion and exclusion criteria, a thorough preanaesthetic evaluation was performed. Prior to study patients were familiarized with the use of Visual Analog Scale (VAS) scoring system.As per the choice of anaesthesiologist and the anaesthetic procedure 30 patients were allocated in each group and either of the drug was given.

GROUP BB: 0.5% Bupivacaine 20 ml + 3µg/kg Buprenorphine + 10ml Normal Saline.

GROUP BM: 0.5% Bupivacaine 20ml + 75 µg/kg Morphine + 10ml Normal Saline.

In preanaesthetic preparation room, standard monitoring for continuous recording electrocardiogram (ECG), noninvasive blood pressure(NIBP), heart rate, and pulse-oxymetry were established and baseline pulse rate, blood pressure, respiratory rate, electrocardiogram, peripheral oxygen saturation were recorded preoperatively. A 20G Intravenous (IV) cannula was established on the contralateral upper limb and IV fluid Ringer's lactate was started. All patients were pre medicated with injection IV glycopyrrolate 0.2 mg and injection IV ondansetron 4 mg before induction.

Patient was positioned supine with folded sheet which was placed below the shoulder to make the field more prominent. Head was turned to 300 to contralateral side. The ipsilateral shoulder shouldc be

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depressed downwards (caudal) and posteriorly by gentle pressure on the shoulder. With sterile aseptic precautions, supraclavicular block was performed by the "Classic Approach,. Interscalene groove was palpated at its most inferior point, posterior to subclavian artery pulsation which was felt in a plane just medial to midpoint of clavicle. Skin wheal raised with local anesthetic solution. 22G, 1 inch needle was inserted caudally. The Shaft of needle and syringe were kept parallel to the plane of head and neck. Needle was directed, aiming at ipsilateral toe and was advanced till paresthesia was felt or muscle contraction of forearm was seen. After negative aspiration, calculated drug (total volume =30 ml) was injected. Oxygen was administered at rate of 3-5 L/min with face mask.

Vital parameters pulse rate, blood pressure, respiratory rate, oxygen saturation, ECG, sensory and motor blockade was monitored in every 5 min. up to 1st 30 minutes, then every 15 minutes up to 1 hour and then at hourly interval up to 6 hours, then 2 hourly up to 12 hours. Complications and side effects of local anesthetic were closely observed. The following parameters were noted- duration of surgery, tourniquet time, onset of sensory block, onset of motor block, duration of sensory and motor block, duration of postoperative analgesia and supplementation with sedation/GA.

Onset of sensory

Time taken from drug injection to pinprick recognition as touch with blunt object. (sensory score 2).

Quality of sensory block assessed in C4 to T2 dermatomes via using following grades.

0 = No loss of sensation to pin prick.
1 = Analgesia (patient feel touch but no pain on pin prick).
2 = Anesthesia (patient even not feel touch sensation on pin prick).

Duration of sensory blockade

Time of onset of block to complete return of paresthesia (sensory score 0).

Onset of motor blockade

Time taken from drug injection to loss of flexion or extension movement in arm and hand against gravity.

Quality of sensory block

By asking the patient to elevate the arm while keeping elbow straight (superior trunk) and at the hand by grip strength (middle and inferior trunk) which were described by Bromage:

0 = no weakness
1 = paresis
2 = paralysis

Duration of motor blockade

Time taken from complete motor blockade to restoration of movements of forearm (grade 0).

Duration of analgesia

Time interval between onset of block to the time of first analgesic consumption.

Post-operative analgesia assessed by 10 point of visual analogue scale
VAS – (VISUAL ANALOUGE SCALE)
0 = no pain
10 = worst pain

The pain score was recorded using the visual analog scale (VAS) 8(T8 h), 10(T10 h), 12(T12 h), 18(T18 h), and 24 (T24 h) after surgery. Significant pain is defined as one that has a score of more than or equal to 4 or above and required a rescue analgesia (injection diclofenac 75 mg IV).

A careful watch was kept for the complication such as-respiratory insufficiency, pneumothorax, diaphragmatic paralysis, respiratory depression, bradycardia, hypotension, headache, convulsions, undesirable sedation, nausea, vomiting, constipation, hematomas and allergic complications like pruritis, itching etc.

Statistical analysis

Considering the duration of analgesia as the main outcome measure of interest. Data was analyzed as mean $\pm$ standard deviation. The onset of sensory block and motor block, duration of sensory and motor block and duration of analgesia were compared using analysis of variance. Statistical analysis was done by graph pad in stat software version 3. Inter group comparison of the quantities data was done using the standard error of difference between two means (t-test). Inter group comparison of qualitative data was done by chi square test. P value < 0.05 was considered as statistically significant.

Results and Observation

Patient characteristics in term of age, sex, weight, and ASA physical status were comparable among the two groups. Duration of surgery was also comparable in two groups. ($p>0.05$). (table 1).

The mean onset of sensory block between two groups was not statistically significant. It was (11.86±1.12 min) in group BB versus (11.76±0.49 min) in group BM. ($p>0.05$).

Time taken for complete sensory block in group BB & group BM (23.83±0.89 vs. 24.03±0.79 min). ($p>0.05$).

The duration of sensory block was significantly longer in group BB (539.67±13.22 min) than group BM (312.26±9.38 min) with $p<0.05$.

The mean onset of motor block was in group BB (8.1±13.22 min) than group BM (8.23±0.61 min). ($p>0.05$).

Time taken for complete motor block in group BB & group BM (27.93±0.67 vs. 28.1±0.39 min). ($p>0.05$).

The duration of motor block was prolonged in group BB (310.67±15.42 min) than group BM (178±9.79 min). $p<0.05$.

The duration of analgesia (i.e., onset of block to perception of pain) was longer in group BB (20.6±2.11 h) than in group BM (13.03±1.32 h) with $p<0.05$.

The pain onset was much earlier in morphine group than that of buprenorphine. That is, mean VAS score 4 at 12th postoperative hour in morphine group. Buprenorphine group has mean VAS score of 4 at 18th hour postoperatively.

First analgesic request was significantly longer in buprenorphine group 18±1.2 h than morphine group 10±2.4 h. The time of rescue analgesia was assessed by VAS score.

Vital parameters like heart rate, systolic blood pressure, SPO2 and respiratory rate all remained within the normal limit after the block in both the groups and did not show any significant difference.

The secondary end point is that no complication occurred with technique owing to opioid and local anaesthetic technique.

Discussion

Perineural administered local anesthetics is an important method to provide pre-emptive as well as it has advantage in postoperative pain management compared to systematically administered drugs[7]. Opioids are valuable adjuvant to local anesthetics due to the prolongation of analgesic effect much beyond the time of surgery. Buprenorphine is an opioid has nonspecific local anesthetic effect. It is a highly lipophilic partial opioid receptor agonist with local anesthetic like property. It is semisynthetic opioid derived from the opium alkaloid thebaine, μ analgesic and k-opioid receptor antagonist[9,10]. It is longest acting opioid and its perineural administration is well established in postoperative analgesia. When administring perineurally acts on peripheral opioid receptors and additionally also block voltage-gated sodium (Na+) channel so that acts as local anesthetic like properties. It decreases K+ ion conduction and increases Ca++ ion conduction in the cell body of neuron, which reduces excitability of nociceptive neuron and accentuate the prolongation of action potential[11]. It also inhibits release of excitatory neurotransmitter substance P from peripheral sensory nerve ending and relief pain. It is estimated that the affinity of buprenorphine for μ receptor is 50 times greater than that morphine, and subsequent slow dissociation from these receptors accounts for its prolonged duration of action leading to lesser requirements of other modalities of analgesia in postoperative period[12].

The objective of this index study was to determine the effects of adding different opioids with equivalent doses to bupivacaine in brachical plexus block with supraclavicular approach. Thus, a perineural injection of 3μg/kg buprenorphine is equipotent to 75μg/kg morphine, but the analgesia produced by buprenorphine lasts significantly longer[9,13].In present study, time for onset of sensory

block and motor block was not statistically significant in both the groups. Mean duration of sensory block was (539.6±13.22 min vs. 312.26±9.38min) and mean duration of motor block was (310.67±15.42 min vs. 178±9.79min) in group BB and group BM respectively. ($p<0.05$). . This prolonged duration appears to be due to the fact that buprenorphine have additional Na+ channels blocking action similar to local anesthetics along with opioids receptors.

We observed difference in postoperative analgesic duration which was significant longer in buprenorphine group (20.6±2.12) h compared to morphine group (13.03±1.32) h with significant p value <0.001. This prolonged postoperative analgesia is because of the fact that buprenorphine is lipid soluble, have high receptor affinity and dissociate very slowly from opioids receptors and clinically reflects as slow offset[14,15]. Moreover, the time of first rescue analgesia was significantly longer in buprenorphine group (18±1.2) h than morphine group (10±2.4) h. The time of rescue analgesia is assessed by VAS score. Total requirement of analgesia was reduced significantly in buprenorphine group compared to morphine group. Moreover, VAS(10, 12, 18, and 24) was lower in buprenorphine group, with p value of 0.001.Various studies reported about the existence of opioids receptors outside the central nervous system and described about peripheral action of opioids. Shaaban A Mousa reported that opioid containing immunocytes migrates to the inflamed sites where they replaces β-endorphin which activates peripheral opioid receptors and produces analgesia[16].The first study, published in 1989 by **Viel EJ et al[17]** observed that the addition of buprenorphine 3µg/kg to 40 ml of 0.5% bupivacaine in supraclavicular brachial plexus block provided almost twice the duration of postoperative analgesia as the addition of morphine 50µg/kg, i.e. a mean of 35 hours as compared with 18 hours. **Bazin et al[18]** obtained similar results in 1997. They also tested buprenorphine as an adjuvant to supraclavicular brachial plexus block and compared it with sufentanil and morphine.

Similarly, in 2001, **Candido KD** and **Winnie AP[18]** had shown that duration of postoperative analgesia following the addition of buprenorphine to the local anesthetic used for brachial plexus block provided a 3 times longer than local anesthetic alone. Encouraged by their results they checked the effect of buprenorphine in case of axillary block. Similarly, **Behr et al** in 2012 demonstrated that the duration of first request for analgesic was twice when buprenorphine was used as adjuvant to local anesthetic as compared to local anesthetic alone. In a recently published study, **Allemano et al[9]** also demonstrated the efficacy of buprenorphine as an adjuvant prolonging the analgesic effect of interscalene brachial plexus block.

According to the results of monitoring, the hemodynamic and respiratory parameters during the anaesthesia no significant difference were observed among two groups in our study. The secondary observation is that no complication occurred with technique owing to opioid and local anaesthetic technique.

Parameter assessed during study

Table 1: Comparison of demographic parameters and duration of surgery

Parameter	Group BB (mean±SD)	Group BM (mean±SD)	P
Age (years)	(33.7±7.16)	(35.2±7.58)	0.5
Weight(kg)	(68.24±5.47)	(69.25±4.60)	0.5
Male:female	24:6	23:7	0.50
Duration of surgery(h)	(2.12±1.04)	(1.60±1.65)	0.14

Table 2: comparison of block characteristics in group BB and Group BM

Variable	Mean±SD (Group BB)	Mean±SD (Group BM)	P
Onset of sensory block (min)	11.86±1.12	11.76±0.49	0.65
Complete sensory block (min)	23.83±0.89	24.03±0.79	0.36
Onset of motor block (min)	8.1±13.22	8.23±0.61	0.95
Complete motor block (min)	27.93±0.68	28.1±0.39	0.24
Quality of sensory block (min)	2.0±00	2.0±00	>0.05
Quality of motor block (min)	1.93±00	2.0±00	>0.05
Duration of sensory block (min)	539.67±13.22	312.27±9.38	0.0001
Duration of motor block (min)	310.67±15.42	178±9.79	0.0001
Duration of analgesia (h)	20.6±2.11	13.03±1.32	0.0001

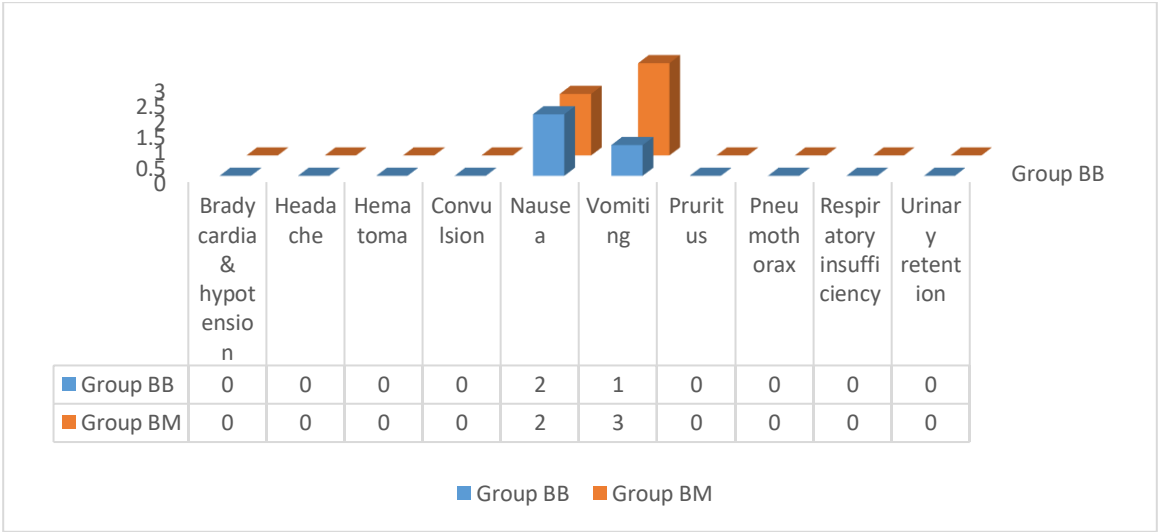

Fig 1:shows that the incidence of nausea vomiting more with morphine.

Conclusion

Buprenorphine added to local anesthetic in supraclavicular brachial plexus block in dose of 3µg/kg provides excellent postoperative analgesia long lasting than morphine. No significant complications of buprenorphine were found when given by peripheral route. Hence, buprenorphine significantly prolongs sensory block and lengthens the duration of analgesia without any systemic complications.

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