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Original Research Article

Comparative Study of Buprenorphine as Adjuvant in PNS Guided Axillary Brachial Plexus Block Vs Placebo

Priyanka Shah[1], Urmi Dave[2], Chetna Jadeja[3]

[1]Senior Resident, Department of Anesthesia, the Gujarat Cancer & Research Institute, Ahmedabad, Gujarat, India

[2]Assistant Professor, Department of Anesthesia, PDU Medical College, Rajkot, Gujarat, India

[3]Associate Professor, Department of Anesthesia, PDU Medical College, Rajkot, Gujarat, India

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Corresponding author: Dr. Chetna Jadeja

Conflict of interest: Nil

Abstract:

Background and Aim: Peripheral administration of opioids has been suggested for prolongation of regional analgesia. Aim of the present study is to evaluate efficacy and safety of Buprenorphine as an adjuvant to Axillary brachial plexus block for post-operative analgesia.

Material and Methods: Present randomized prospective double blind controlled trial was performed at P.D.U. Medical College, Rajkot in 50 Adults. Each patient was randomly allocated to one of two groups of 25 patients each. Group C receives 15 ml Lignocaine + Adrenaline 1.5%- and 15-ml Bupivacaine 0.5% diluted upto 1ml of normal saline while Group B receives 15 ml Lignocaine + Adrenaline 1.5%- and 15-ml Bupivacaine 0.5% and Buprenorphine 3 mcg/kg diluted upto 1ml normal saline. Onset, duration of sensory and motor block, hemodynamic parameters, sedation score, and pain scores using visual analog scale, duration of postoperative analgesia, rescue analgesic (RA) requirement, adverse events, and patient satisfaction were noted.

Results: Both groups were comparable in demographic parameters. Onset and duration of sensory and motor block was similar in both groups. B group had significantly higher VAS scores compared to C group ($P \leq 0.05$). Duration of analgesia was the higher in B (20.39±1.22) Compared to in Group C (10.88±0.74) ($P < 0.05$).

Conclusion: Buprenorphine 3 mcg/kg in axillary plexus block provides significantly prolonged analgesia with less RA requirement and greater patient satisfaction compared to Placebo groups.

Keywords: Axillary Brachial Plexus Block, Buprenorphine, Duration of analgesia, Rescue Analgesic.

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Introduction

The Axillary brachial plexus block is good anaesthesia alternative for provide forearm and hand surgery. Peripheral administration of opioid has been suggested for prolongation of regional anaesthesia. Buprenorphine has been used as an adjuvant to local anesthetics to prolong the duration of effect of local anaesthetics drugs. Buprenorphine is semisynthetic opioid. Buprenorphine is 30 time more potent than morphine. Buprenorphine partial mu agonist & kappa antagonist.

We decided to evaluate efficacy of Lignocaine + Adrenaline 1.5% and bupivacaine 0.5% Axillary brachial plexus block in upper limb surgeries and its clinical comparison lignocaine + Adrenaline 1.5% and bupivacaine with Buprenorphine 3 mcg/kg via Axillary approach under PNS guidance. [1,2] Initial experimental studies by Stein C ^3 et al on rats have demonstrated the presence of opioid receptors on primary afferent neuron and peripheral sensory nerve fiber by immunocytochemical methods. It is worth administering opioid in the brachial plexus block only if it provides better and longer duration of anaesthesia with lesser side effect. Addition of Buprenorphine as adjuvant with local Anaesthetic drug is well accepted. So we decided to evaluate efficacy of Buprenorphine with Local anaesthetics in PNS guided brachial plexus block via axillary approach. [3-6]

Aim of the present study is to evaluate efficacy and safety of Buprenorphine as an adjuvant to Axillary brachial plexus block for post-operative analgesia.

Material and Methods

Present randomized prospective double blind controlled trial was performed at P.D.U. Medical College, Rajkot from March 2021 to March 2023. Randomization was done with computer generated random number table. Blinding was done with use of sealed envelope which contain computer generated numbers. Odd number indicate group C

and even number indicate group B. Sealed envelopes will be given to anesthesiologist anaesthetizing the patient which will be revealed in operating room.

Sample size calculation: The sample size is decided in consultation with statistician and is based on pilot study observations, indicating that approximately patients should be included in each group in order to ensure a power of 0.80. This would permit a type 1 alpha error = 0.05, with a type 2 error of beta =0.2.

Study was consisting of patients of both genders belonging to ASA I to IV, who were undergoing upper limb surgeries under Axillary brachial plexus block.

Inclusion Criteria

1. Patients aged between 18- 60 years
2. Physical status ASA grade I, II ,III
3. Scheduled for upper limb surgeries

Exclusion Criteria

1. Other than ASA grade IV and above
2. Known allergy to local anaesthetic agents and opioids
3. Local infection at site of block
4. Brachial plexus injury
5. Neuromuscular diseases
6. Bleeding disorders or patient on anticoagulant therapy
7. Pregnancy

Study Group: Each patient was randomly allocated to one of two groups of 25 patients each

Group C: Receives 15 ml Lignocaine + Adrenaline 1.5%- and 15-ml Bupivacaine 0.5% diluted upto 1ml of normal saline

Group-B: Receives 15 ml Lignocaine + Adrenaline 1.5%- and 15-ml Bupivacaine 0.5% and Buprenorphine 3 mcg/kg diluted upto 1ml normal saline.

All necessary equipment's and drugs needed for administration of general anaesthesia to be kept ready in order to manage failure of block.

Each patient was visited pre-operatively, investigated, procedure explained and written informed consent will be obtained. Intravenous access is obtained. Standard multipara monitor monitors ECG, pulse oximeter, non-invasive blood pressure to be applied and monitored and recorded at interval of 5 minutes in the first hour and every 15 minutes thereafter. Premedication was given to patient as Inj. Ondansetron 1 mg/kg, Inj. Midazolam 1 mg/kg. The arm to be blocked was abducted to 90 degrees. After applying all the standard, the arm to be blocked will be abducted to 90 degrees, externally rotated and hand supinated.

Under all aseptic precautions, axillary block was performed with 22G insulated needle and a nerve stimulator. In group B 15ml (1.5%) lignocaine + adrenaline + 15ml (0.5%) bupivacaine + 3mcg/kg buprenorphine diluted upto 1ml normal saline total 31ml of drug was prepared out of which 10 ml will be given after production of characteristic motor response of biceps contraction on stimulation of musculocutaneous nerve at 0.4mA, 10ml was given after production of characteristic motor response of finger flexon on stimulation of ulnar nerve at 0.4mA, 10ml was given after production of characteristic motor response of finger extension on stimulation of radial nerve at 0.4mA. Thus total 30ml of local anaesthetic was given including buprenorphine. In group C same concentration and volume of local anaesthetic was be given but in place of inj. Buprenprphine same volume of normal saline was given. Onset time for sensory and motor block was taken as time between injection and loss of sensation in 3 nerve distribution by pinprick test and loss of flexion /extension movement in forearm or hand against gravity, respectively.

Duration of sensory block was considered as time from complete sensory block to return of paraesthesia. Duration of motor block was considered from time between complete motor block to restoration of the full hand and wrist mobility.

Hemodynamic parameters (heart rate,systolic blood pressure), respiratory rate and Spo2 was monitored every 10 min intraoperatively. Postoperatively, same parameters except Spo2 was be monitored every hourly for first 8 h.

Pain assessment was done using visual analog score (VAS) scale (0-no pain to 10-worst pain). Time between block administration and onset of pain (VAS 4) was taken as duration of analgesia. VAS assessment was taken every hour to first 8 h then 2 hourly for 24 h and 4 hour up to 36 h in awake patients. Rescue analgesia (RA) in the form of injection PCM 15 mg/kg. Given at VAS 4. Next dose of RA was repeated after 8 h if required. Requirement of RA 36 h noted.

Sedation score were graded on a simple scale as: 0 – fully alert; 1 – alert quiet, obeys verbal commands; 2 –sleepy but prompt response to verbal commands; 3 – sleepy but prompt response to light glabellar tap; 4 – sleepy, responding only to firm glabellar tap. Sedation score assessed at every hour for first 12 h. adverse effects like hypotension, bradycardia, nausea, vomiting, respiratory depression, pruritus, urinary retention was noted. At the end of 36 h, patients' satisfaction for pain relief graded as: Excellent, good, fair, poor.

Accidental systemic administration of buprenorphine is associated with sedation and post-operative nausea, vomiting. [2,3,4] Lignocaine +

Adrenaline is as such least cardiotoxic among all local anaesthetic drug. Along with Buprenorphine, it prolongs duration of analgesia with better haemodynamic stability.

Statistical Analysis: Repeated measures of ANOVA for vital parameters and Student's t-test for onset, duration of sensory and motor block. P value <0.05 is considered significant & p value <0.001 is considered highly significant. Data will be expressed as mean± SD or % as appropriate.

Results

Both groups were comparable in demographic parameters [Table 1]. Onset and duration of sensory and motor block was similar in both groups [Table 2]. Hemodynamic parameters (peak rise in pulse rate and blood pressure) were corresponding with VAS scores. B group had significantly higher VAS scores compared to C group (P≤0.05).

Duration of analgesia was the higher in B (20.39±1.22) Compared to in Group C (10.88±0.74) (P < 0.05) [Table 2]. In group B one patient had nausea and rest all were free from any side effects. Whereas, in C group 3 patients had nausea and 4 had vomiting (P > 0.05).

Table 1: Demographic data

Variable	Group B (n=25)	Group C (n=25)	P value
Age (years)	28.50±5.12	28.30±4.38	0.22
Gender (male: female)	13:12	12:13	0.09
Weight (kg)	57.90±5.22	57.31±5.28	0.48
Duration of surgery (h)	2.10±0.3	1.90±0.40	0.34

Statistically significance at p≤0.05

Table 2: Onset, duration of block, duration of postoperative analgesia and adverse effects

Time	Group B (n=25)	Group C (n=25)	P value
Onset of sensory block (min)	3.70±0.62	3.80±0.47	**0.41**
Onset of motor block (min)	6.79±0.74	7.22±0.61	**0.23**
Duration of sensory block (h)	5.38±0.39	5.41±0.44	**0.31**
Duration of motor block (h)	4.69±0.22	4.78±0.56	**0.22**
Duration of analgesia (h)	20.39±1.22	10.88±0.74	**0.002***

Discussion

Brachial plexus block with LAs has been used for upper limb surgeries. Additives such as adrenaline, α-2 agonists, neostigmine, and opioids have been investigated for prolongation of analgesia. Initial experimental studies by Field et al. [7] on rats have demonstrated the presence of opioid receptors on primary afferent neurons and peripheral sensory nerve fibers by immunocytochemical methods. Although the presence of peripheral receptors in human has been well documented, their mechanism of action remains unclear. [8]

The proposed antinociceptive actions of peripherally administered opioids include a nonspecific, LA like effect. This includes a decrease in K+ conduction and an increase in Ca++ conduction in the cell body of sensory neuron. This reduces excitability of the nociceptive neuron. Opioids also inhibit the release of excitatory neurotransmitter substance P from the peripheral sensory nerve endings. They may have central action caused by centripetal movement via opioid binding proteins from periphery to the dorsal horn. It is worth administering opioid in the plexus block only if it provides better and longer duration analgesia with lesser side effects compared to systemically administered drug. Salient features of buprenorphine namely, long duration of action, lipophilic nature, high affinity for μ-receptor as compared to other opioids and ceiling effect on respiratory depression has further stimulated the research in this area. Moreover, it is freely available and cost effective.

From 2001 onward, eight studies [9-12] have reported significantly long duration of analgesia using buprenorphine in brachial plexus block. However, only three [9,13,14] out of eight studies had systemic control group. Rest five studies had placebo control group where plain LAs were used for the block. In 2008, Jadon et al [14] studied the effect of the addition of 3 g/kg buprenorphine to 0.3% bupivacaine in subclavian perivascular block.

Our study showed significantly longer duration of analgesia and reduced requirement of RAs with buprenorphine addition in axillary plexus block compared to IM administration. This is additional evidence supporting peripherally mediated analgesic action. The results of the present study demonstrated that the addition of buprenorphine to 15-ml Bupivacaine 0.5 % undergoing upper limb surgeries under Axillary brachial plexus block. Provides prolonged duration of analgesia post LPB, longer pain free interval, decreased pain (VAS) score, and reduced analgesic requirement.

Buprenorphine interacts with the opioid receptor-like (ORL1) receptor, which has distinct

pharmacological characteristics, activation of which leads to inhibition of the enzyme adenylate cyclase, calcium channel conductance, and activation of inwardly rectifying potassium channels. [15,16] The analgesic effect of buprenorphine is the effect of the suppression of spinal synaptic transmission by alteration of these two ion channels. The intense action of buprenorphine peripherally is a potent property of buprenorphine as a local anesthetic is by binding to intramembranous part of receptor; it mediates the tonic and concentration dependent blockade of Na+ channels, thus blocking action potential in the terminal endings of C fibers. This property is greater than other opioids and several local anesthetics. prenorphine as an adjuvant in various peripheral nerve blocks with encouraging results. [17,18] Studies on the use of buprenorphine in lumbar plexus block were, however, lacking. Hence, we intended to study the effect of buprenorphine as an adjuvant to levobupivacaine in ultrasound-guided lumbar plexus block for postoperative analgesia in patients undergoing surgeries around the hip, thigh, and knee, under the subarachnoid block, simultaneously also comparing two different doses of buprenorphine viz. 150 μg and 300 μg to determine the optimal dose.

Buprenorphine via axillary plexus block can act by: (1) Systemic absorption, (2) spread to central neuraxis, and (3) direct action on peripheral opioid receptors on plexus nerves. In our study regionally administered buprenrphine provided 20.39±1.22 h of analgesia compared to 10.88±0.74 h of analgesia by IM route. This makes systemic absorption as unlikely mechanism. Spread to central neuraxis is also unlikely mechanism as brachial plexus was blocked by axillary approach, a distant site from spinal cord. Furthermore, the drug selected for trial – buprenorphine, is lipophilic and has high affinity for -receptor and hence unlikely to get transported to spinal cord. Hence, most likely site of action is at peripheral opioid receptors on plexus nerves. In a study by Candido et al [9] incidence of vomiting in the systemic group was 25% compared to 5% in the regional group. Jadon et al [14] study had a similar incidence of vomiting in both groups. In our study, 17.4% of patients had vomiting in the systemic group compared to none in the regional group. This again emphasizes the importance of regional administration of buprenorphine.

Although the actual neurophysiochemical mechanism is speculative, the present study provides the convincing evidence of benefits of adding buprenorphine to LA solutions for upper extremity blocks in day care surgeries. Further work is needed to define the mechanism of peripheral action of opioids. A dose-finding study with lower doses for buprenorphine in axillary block may be done to determine maximum beneficial effects at lower doses.

Conclusion

Buprenorphine 3 mcg/kg in axillary plexus block provides significantly prolonged analgesia with less RA requirement and greater patient satisfaction compared to Placebo groups.

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