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

[1]Surendra Raikwar, Professor, Department of Anaesthesiology, Gandhi Medical College, Bhopal, India

[2]Jaideep Singh, Associate Professor, Department of Anaesthesiology, Gandhi Medical College, Bhopal, India

[3]Preeti Verma, Junior resident 3rd year, Department of Anaesthesiology, Gandhi Medical College, Bhopal, India

[4]Kirti Sisodiya, Junior resident 3rd year, Department of Anaesthesiology, Gandhi Medical College, Bhopal, India

Corresponding Author: Preeti Verma, Junior resident 3rd year, Department of Anaesthesiology, Gandhi Medical College, Bhopal, India

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Abstract

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 used as an adjuvant to prolong analgesia with local anesthetic. Aim of study to evaluate the quality and duration of postoperative analgesia by adding buprenorphine and morphine to local anesthetic solution. 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 RB (buprenorphine group) received: 0.5% Ropivacaine 30 ml + 3µg/kg Buprenorphine. Group RM (morphine group) received: 0.5% Ropivacaine 30ml + 75µg/kg Morphine. The parameters observed were onset and duration of sensory and motor block, quality and duration of analgesia and side-effects. The mean duration of postoperative analgesia was significantly longer in group BB (20.33±2.27hrs) than in group BM (12.36±2.17hrs) with $p<0.05$. 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 RB (586.17±38.67mins) than in group RM (376.26±46.12mins) with $p<0.05$. The mean duration of motor block was prolonged in group RB (360.33±60.26mins) than in group RM (284.07±83.60mins) with $p<0.05$. Thus, addition of 3µg/kg buprenorphine to 0.5% ropivacaine for supraclavicular brachical plexus block prolonged duration of postoperative analgesia, duration of sensory and motor blockade than morphine without an increase in side effects.

Keywords: Buprenorphine, morphine, ropivacaine, supraclavicular brachical plexus block.

Introduction

The perception of pain is a complex phenomenon that is influenced by the emotional state and past experiences of individual. Regional anesthesia is one in all the well-known anesthesia technique that has some additional benefits when put next to general anesthesia[1–4].

Regional nerve block not solely eliminate the pain however additionally facilitate surgery and attenuate the pain that follows postoperatively. The brachial plexus block with local anesthetics is one in all the foremost unremarkably used regional nerve block technique for upper limb surgeries to their high success rate and skill to produce prolonged operative pain relief[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. A rang of adjuvant drugs are tried with local anesthesia to prolong intraoperative and postoperative analgesia[6].

Peripheral opioid administration as adjuvants to local anesthetic drugs for regional anesthesia improves quality and duration of brachial plexus block and additionally prolongs postoperative analgesia without side effects[7]. Moreover the dose and amount of local anesthetic drugs are also reduced. Our main aim in analgesic analysis is to obtain agents with desirable analgesic properties, free from its side effects.

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 surgery.

Materials and methods

After approval from the ethics committee a prospective, observational study was conducted in department of anesthesiology, GMC Bhopal and associated Hamidia hospital from. October 2019 to December 2019, in accordance with Helsinki Declaration of 1975, as revised in 2000.Written informed consent was obtained and patient related confidentiality was maintained.

Sixty patients of ASA grade I and II of age group between 18yrs-45yrs of either sex were included in our study undergoing upper limb surgeries. Non-consenting patients, patient with 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/E were excluded from the study. After satisfying inclusion and exclusion criteria, a thorough preoperative evaluation was performed. The patient was briefed about the supraclavicular block to be performed, its advantages over general anesthesia and also about the associated complications. Informed consent was obtained from every patient prior to the study, and they were familiarized with the use of Visual Analog Scale (VAS) scoring system. Sensitivity testing was done for lignocaine in all patients, and the patients were kept fasting 6 hours prior to surgery.

Patients were allocated into two groups with each group consisting of 30 patients.

GROUP RB: 0.5% Ropivacaine 30 ml + 3µg/kg Buprenorphine.

GROUP RM: 0.5% Ropivacaine 30ml + 75µg/kg Morphine.

All patients underwent thorough general clinical examination prior to starting the surgery. Monitors were attached before performing the procedure for continuous recording of noninvasive BP, heart rate, electrocardiogram and SpO2. Baseline pulse rate, blood pressure, respiratory

rate, electrocardiogram, peripheral oxygen saturation was recorded preoperatively. Intravenous (IV) access was established on the contralateral upper limb and secured with 20G teflon cannula and IV fluid ringer lactate was started. All patients included in the study received injection glycopyrrolate 0.2 mg IV and injection ondansetron 4 mg IV as premedication.Whole procedure was explained to all patients in their own language for their complete cooperation.Patient was kept in supine position with head turned to opposite side and arm pulled down gently blocked adducted and kept by the side. A small pillow or folded sheet was placed below the shoulder to make the field more prominent.After sterile preparation of the region supraclavicular block was performed by the "Classic Approach," which was first described by Kulenkampff in 1911. Aftertaking all aseptic precautions, an intradermal wheal with 2% lignocaine plain at the selected point was raised. A hypodermic needle of 22 G of 1 inch was inserted through the wheal directed medially and inward at the angle of 20 degree to the skin until the paresthesia elicited in the hand. After negative aspiration, calculated drug was injected. Oxygen was administered at rate of 3-5 L/min with face mask.

Vital parameterspulse rate, blood pressure, respiratory rate, oxygen saturation, ECG, sensory and motor blockade 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 complete ablation of sensation (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 complete motor block (motor grade score 2).

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

All data analysis were compiled in the form of mean and 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. Further analysis was performed using unpaired t-test. $P < 0.05$ was considered as statistically significant.

Results

Both the groups were comparable with regards to age, ASA physical status, sex ratio, weight, duration and type of surgery (table 1). The mean onset of sensory block between two groups was not statistically significant. It was (8.60±2.16 min) in group RB versus (9.16±2.76min) in group RM with $p>0.05$.

The duration of sensory block was significantly longer in group RB (586.17±38.67 min) than group RM (376.26±46.12 min) with $p<0.05$.

The mean onset of motor block was in group BB (16.30±4.08 min) than group BM (17.48±4.21 min) with $p>0.05$.

The duration of motor block was longer in group RB (360.33±60.26 min) than group RM (284.07±83.60 min) with $p<0.05$.

The duration of analgesia (i.e., onset of block to perception of pain) was longer in group BB (20.33±2.27 h) than in group BM (12.36±2.17 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 18th postoperative hour in morphine group where as it was only (3±0.5) at 18th postoperative hour in buprenorphine group. Buprenorphine group has mean VAS score of 4 at 24th 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

The overall objective of conducting this study was to determine the effect of adding 3µg/kg buprenorphine and 75µg/kg morphine based on, set equipotency of the drugs as an adjuvant to local anesthetic in brachial plexus block with supraclavicular approach. Thus, an intravascular injection of 3µg/kg buprenorphine is equipotent to75µg/kg morphine, but the analgesia produced by buprenorphine lasts significantly longer[8]. This prolonged duration appears to be due to the fact that buprenorphine seems to dissociate very slowly from opioids receptors, so that the usual duration of action is 8 hours following parenteral administration[9,10].

Supraclavicular brachial plexus block is a simple, safe and commonly performed regional anesthetic technique. It provides anesthesia to the patients undergoing upper extremity surgery, and good pre-emptive as well as postoperative analgesia.

Commercial bupivacaine is a racemic mixture of (R)- and (S)- stereoisomerism. In response to problem of high lipophilicity causes cardiovascular toxicity resulting from accidental intravenous injection of bupivacaine. Ropivacaine is a single (S)- stereoisomer were formulated

to exploit this stereoselectivity. The slow reversal of Na^+channel blockade after a cardiac action potential, which is a hallmark of bupivacaine, is considerably faster with ropivacaine. In addition to these electrical differences, the negative inotropic potency of ropivacaine on isolated cardiac tissue appears to be considerably less than that bupivacaine[8,9]. Hence, we preferred ropivacaine over bupivacaine in our study.

Various opioids have been tried successfully as adjuvants in peripheral nerve blocks. Buprenorphine is an agonist-antagonist, semi-synthetic opioid derived from the opium alkaloid thebaine, highly lipid-soluble μ analgesic and k-opioid receptor antagonist. It is estimated that the affinity of buprenorphine for μ receptors 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[8–10].

In our study, the mean time of onset of sensory blocked was (8.60±2.16) min in buprenorphine group compared to morphine group (9.16±2.76) min while onset of motor blockade for buprenorphine and morphine group was (16.30± 4.08) min and (17.48± 4.21) min respectively with P value > 0.05 which showed that time of onset of sensory and motor blockade was not statistically significant in both the group. There is no mechanism of opioid that explains this decreased onset of sensory and motor block.

The mean duration of sensory block was significant prolonged in buprenorphine group (586.17±38.67) min compared to morphine group (376.26±46.12) min. These changes were statistically significant when compared to each other ($p \leq 0.05$). Duration of motor block was also significant prolonged in buprenorphine group (360.33±60.26) min compared to morphine group (284.07±83.60) min with p value was <0.05.This is due to when buprenorphine given perinurally acts on peripheral opioid receptors and Na^+channels similar to local anesthetics[8]. The quality of motor block was complete in 100% of patients receiving morphine and 94% of patients receiving buprenorphine.

There was significant difference in postoperative analgesic duration which was significant longer duration in buprenorphine group (20.33±2.27)hrs than in morphine group (12.36±2.17)hrs with p value <0.05. Moreover, the time of first rescue analgesia was significantly longer in buprenorphine group (18±1.2)hrs than morphine group (10±2.4)hrs. The time of rescue analgesia as 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.

It has been studied that perinurally administration of opioids exerts their analgesic effect through both central and peripheral mechanism. This can be explained by core and mental concept described by Winneet al. cellular mechanisms of action G-protein-coupled receptors, such as those for opioids, have no direct link with effector proteins; instead the message is relayed via a G protein. Both classical opioid receptors (MOP/ KOP/DOP) and the non-classical NOP opioid receptor couple to inhibitory G-proteins. Activation of opioid receptors, for example MOP with opioids leads to: (i) closing of voltage sensitive calcium channels (ii) stimulation of potassium efflux leading to hyper polarization; and (iii) reduced cyclic adenosine monophosphate (cAMP) production via inhibition of adenylyl cyclase. Overall, this results in reduced neuronal cell excitability leading to a reduction in transmission of nerve impulses along with inhibition of neurotransmitter release.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 activates peripheral opioid receptors and produces analgesia[11].

Similar to our results, a study done by **Viel EJ et al**[12] observed a significant difference in the quality of analgesia was found and was superior with 3µg/kg buprenorphine as compared with 50µg/kg morphine added to local anesthetic. The duration of analgesia was nearly twice as long in the buprenorphine group as in the morphine group (35.05±1.95 h) versus (18.25±1.15 h). Similarly, **J. E. Bazin et al**[13] obtained similar results**.** They also tested buprenorphine as an adjuvant to supraclavicular brachial plexus block and compared it with sufentanyl and morphine. As per **Kinjal S et al**[14] and **Surekha Patil et al**[15] concluded that addition of buprenorphine to local anaesthetic drug provided good postoperative analgesia. Similarly, **Jain N et al**[16] studied that on addition of 0.3mg buprenorphine to 0.5% ropivacaine 30 ml, prolongs the duration of sensory block, motor bock and analgesia significantly, without increasing adverse effects.

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. Since buprenorphine has a ceiling to its effect at and above the ceiling dose response curve, remains flat limiting its effect, while morphine continues to increase effects until patient succumbs to respiratory depression.[12]

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

Table 1: Comparison of demographic parameters and duration of surgery

Parameter	Group RB (mean±SD)	Group RM (mean±SD)	P-value
Age (years)	(33.7±7.16)	(35.2±7.58)	0.5
Weight(kg)	(69.24±5.47)	(70.25±4.60)	0.44
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 RB and group RM

Variable	Mean±SD (Group RB)	Mean±SD (Group RM)	P-value
Onset of sensory block (min)	8.60±2.16	9.16±2.76	0.38
Onset of motor block (min)	16.30±4.08	17.48±4.21	0.27
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)	586.17±38.67	376.26±46.12	0.0001
Duration of motor block (min)	360.33±60.26	284.07±83.60	0.0002
Duration of analgesia (h)	20.33±2.27	12.36±2.17	0.0001

Table 3: Mean Visual Analog Score At Different Time Intervals

Time (HRS)	Group RB VAS (MEAN±SD)	Group RM VAS (MEAN±SD)
8	0.2±0.4	0.9 ± 0.77
10	1.4±0.5	2.17 ± 0.78
12	2.2±0.6	3.9± 0.67
18	3±0.5	4±0.68
24	4±0.4	4.8±0.6

Table 4: Comparison of complication

Complication	Group RB	Group RM
Bradycardia & hypotension	0	0
Headache	0	0
Convulsion	0	0
Nausea	2	3
Vomiting	1	1
Pruritus	0	0
Pneumothorax	0	0
Respiratory insufficiency	0	0
Urinary retention	0	0

Conclusions

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 as compared to systemic route. Hence, buprenorphine significantly prolongs sensory block and motor block, contributing to lengthens the duration of analgesia.

Abbreviations

ASA- American society of anaesthesiologist, yrs-years, VAS-visual analogue scale, BP-blood pressure, ECG-electrocardiogram, mins-minutes, hrs-hours, mmHg-millimeter of mercury, kg-kilogram, h-hours.

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