

## Comparative study of bupivacaine alone and bupivacaine along with buprenorphine in axillary brachial plexus block: a prospective, randomized, single blind study

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### ABSTRACT

**Background:** Different additives have been used to prolong brachial plexus block. We performed a prospective, randomized single-blind study to compare Bupivacaine alone and Bupivacaine along with Buprenorphine for onset, quality, and duration of block as well as post-operative analgesia and any complication in axillary brachial- plexus block.

**Methods:** Randomized controlled study was carried out among 60 patients of either sex, aged 20-60 years. ASA grade I or II undergoing elective hand, forearm, elbow surgery under axillary brachial plexus block. Patients were randomly divided into two groups.

Group-I received 30 ml of 0.35% Bupivacaine alone in axillary block.

Group-II received 30 ml of 0.35% Bupivacaine with 3µg/kg Buprenorphine in axillary block. Time taken for onset and completion of motor and sensory block as well as complete duration of block were noted in both groups. Any complication during procedure, during surgery as well as post-operatively were noted and treated.

**Results:** Addition of Buprenorphine (3µg/kg) to Bupivacaine mixture in peripheral nerve block did not affected the onset time for motor as well as sensory block. Mean duration of motor block was 284.33±78.94 mins. in group I and in group II 307.33±60.26 mins. Mean duration of sensory block 305.066±83.64 mins. in group I while 580.166±111.45 mins. in group II. It suggests duration of sensory block was prolonged in group II then group I.

**Conclusions:** Addition of Buprenorphine to local anesthetic drug provides good post-operative analgesia. Buprenorphine significantly prolongs sensory block and lengthens duration of analgesia without prolonging duration of motor block.

**Keywords:** Bupivacaine, Buprenorphine, Axillary block, Sensory and motor block

### INTRODUCTION

Pain is subjective phenomenon, it is perceived only by the sufferer, while the observer can only assess its intensity. Feeling of pain by the patient is an insult to the dignity of an anaesthesiologist. Satisfactory pain relief has always been a problem in clinical practice.

Narcotic analgesics are still indispensable for the treatment of severe pain and major objective in analgesic research to obtain agent with desirable analgesic properties but free from its side effects, like respiratory depression, addiction and gastro-intestinal disturbance. Morphine is thought to produce its effect by action on specific receptors in the dorsal horn of spinal cord and on central opioid receptors.<sup>1</sup> Recent reports have suggested that morphine injected perineurally in patients with

chronic pain may also have a clinically significant effect and its duration of action may be longer than that of systemically administered morphine or nupivacaine.<sup>2</sup> Sanchez et al proposed the neuro-axonal transport of morphine to the spinal cord as an explanation for this effect.<sup>3</sup> Other mechanism that have been put forward are; a local anesthetic like action or direct effect of morphine on stereo-specific opioid receptors on the cell membranes of peripheral nerve axons.<sup>4</sup> Like morphine, buprenorphine does not have a linear dose response curve. At very low doses (<0.5 mg) buprenorphine is 20-50% as potent as morphine. Because 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.<sup>5-9</sup> Buprenorphine is liposoluble, longer acting and when used in peripheral nerve block

have less systemic side effects. So we decided to study buprenorphine as an adjuvant to bupivacaine in axillary block.

Buprenorphine is N-cyclopropylmethyl oripavine-semisynthetic thebaine derivative. It is highly lipophilic and has both opioid agonist-antagonist properties. Buprenorphine has high affinity for both mu and kappa receptors and low to moderate intrinsic activity at mu and kappa receptors. It shows affinity for delta receptors with low intrinsic activity.<sup>5</sup> Opioid containing immunosites migrate to the inflamed sites where they release  $\beta$ -endorphin which activates peripheral opioid receptors and produce analgesia.<sup>6</sup> Preliminary clinical trials in men have shown that Buprenorphine is safe, potent and long lasting narcotic analgesic useful for postoperative pain relief.

Bupivacaine is long acting amide local anesthetic agent commonly used in peripheral nerve block. The base is not soluble but the hydrochloride salt readily dissolves in water. Pka is 8.2. It is available in bulb with 0.5%, 0.25% and 0.75 %.

Opioids are used as an adjuvant to prolong its action for post-operative analgesia. Various studies on the benefit of adding analgesic adjuncts to brachial plexus block have shown mixed results.<sup>7</sup> This practice can be of particular benefits to the patients undergoing ambulatory upper extremity surgery providing prolonged analgesia even discharge from hospital. Nowadays various newer opioids are available like fentanyl, but buprenorphine is longer acting than fentanyl and when used in peripheral block have less systemic side-effects.

## METHODS

A randomized controlled single blind study was carried out in 60 patients of either sex, aged 20-60 years, ASA grade-I or II, posted for elective hand, forearm and elbow surgery under axillary brachial plexus block. Patients with uncontrolled diabetes mellitus or hypertension, peripheral neuropathy, hepatic or renal disease, pregnant patients and known allergy or hypersensitivity to local anaesthetic drugs were excluded from the study. Patients were explained about procedure & complication, informed consent was taken. Patients were randomly assigned to one of the two groups, each containing 30 patients.

On arrival to the operating room, patients baseline vitals like heart rate, blood pressure, oxygen saturation and respiratory rate were recorded. Intravenous crystalloid was started. Patients were pre-medicated with inj. midazolam 0.01 mg/kg, intravenously. Supine position was given to the patient with arm abducted and elbow flexed at 90 degrees and externally rotated at shoulder leaving the arm lying across the patient's head. After aseptic precaution, first axillary artery pulsation was palpated as high as possible in axilla. A 23 G and 1.5 inch needle was inserted slowly at about 30 degrees to the skin

towards the side of artery and loss of resistance of sheath was felt, at the same time also confirmed by paresthesia. Correct placement in the sheath was also confirmed by pulsation of needle indicating close proximity to the artery. Drug was injected with repeated aspiration to avoid inadvertent intravascular injection. Then firm pressure was placed over sheath below the point of injection and solution was encouraged towards the axilla and tourniquet was applied. Group-I received 30 ml of 0.35% bupivacaine while Group-II received 30 ml of 0.35% bupivacaine with 3 $\mu$ g/kg buprenorphine in axillary brachial plexus block. An anaesthesiologist not involved in performance of brachial plexus block did evaluation. Evaluation was carried out after 5 minutes of completion of injection and time of onset was noted for both motor and sensory effects. Sensory block was tested by sensation to pin-prick, and motor block 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.

### Hollmen Scale<sup>8</sup>

#### Sensory block

| SCALE |  |
|-------|--|
| 1     | Normal sensation of pinprick.  |
| 2     | Pinprick felt as sharp pointed but weaker compared with same area in other limb. |
| 3     | Pinprick recognized as touch with blunt object.                                  |
| 4     | No perception of pinprick.   |

#### Motor block

| SCALE |                                 |
|-------|---------------------------------|
| 1     | Normal muscle function.         |
| 2     | Slight weakness in function.    |
| 3     | Very weak muscular action.      |
| 4     | Complete loss of muscle action. |

*Onset of block:* Defined as minimum of grade 3 for sensory and grade 3 for motor of Hollmen scale.

*Complete block:* When sensory and motor scores were 4 in Hollmen scale.

Duration of sensory block was considered as the time interval between Hollmen scale 3 to onset of pain in post-operative period.

Duration of motor block was considered from Hollmen scale 3 to recovery of muscle power.

**Failed block:** When separate nerve block or supplementation with intravenous analgesic or general anesthesia was required, considered as an inadequate or failed block.

Intra operative complications like, arterial puncture, nausea, vomiting, allergic reaction, inadequate block or serious complication like convulsion, respiratory arrest were recorded.

Patients were continuously monitored intra-operatively by recording vitals every 15 minutes for half an hour, then every 30 minutes till surgery was completed, then hourly post-operatively.

## RESULTS

The demographic characteristics with sex distribution, age, weight, ASA grade, type of surgical procedures are detailed in Table 1.

**Table 1: Demographic data.**

|                           | Group I  | Group II |
|---------------------------|----------|----------|
| Age (yrs.)                | 20±10.73 | 20±9.18  |
| Weight (kg)               | 42±7.84  | 41±7.82  |
| Sex - M:F                 | 22:8     | 18:12    |
| ASA grade 1:2             | 17:13    | 19:11    |
| Duration of surgery(mins) | 39±39.40 | 45±39.73 |
| Unsuccessful block (n)    | 2        | 1        |

Values are expressed as mean±SD. There are no significant differences between groups.

Table 2 shows that mean onset time for motor anesthesia is 8.033±2.40 mins. in group-I while in group-II it is 8.216±1.66 mins. P value is >0.05, so it is insignificant. Mean onset time for sensory anesthesia is 12.8000±4.32 mins. in group I while in group-II it is 12.1167±2.70 minutes. It shows P value>0.05, so it is insignificant. It suggests addition of buprenorphine to local anesthetic drug does not affect time of onset of block.

**Table 2: Mean time for onset of block.**

| Time                 | Block   | Group I          | Group II         | P value |
|----------------------|---------|------------------|------------------|---------|
| Mean<br>± SD (mins.) | Motor   | 8.0333<br>±2.40  | 8.2167<br>±2.66  | 0.73    |
| Mean<br>± SD (mins.) | Sensory | 12.8000<br>±4.32 | 12.1167<br>±2.70 | 0.46    |

**Table 3: Mean of time taken for complete block.**

| Time        | Block   | Group 1         | Group 2        | P value |
|-------------|---------|-----------------|----------------|---------|
| Mean<br>±SD | Motor   | 28.40<br>±8.22  | 29.76<br>±6.29 | 0.47    |
| Mean<br>±SD | Sensory | 24.60<br>±10.39 | 29.10<br>±7.85 | 0.06    |

Table 3 shows mean time taken for complete motor block in group I and II (28.40±8.22 / 29.76±6.29 minutes), while for complete sensory anesthesia group II required more time as compared to group I (24.60±10.30/29.10±7.85 mins). In both p value is >0.05, so it is insignificant.

**Table 4: Duration of anesthesia.**

| Time                    | Block   | Group I           | Group II           | P      |
|-------------------------|---------|-------------------|--------------------|--------|
| Mean<br>± SD<br>(mins.) | Motor   | 284.33<br>±78.94  | 307.33<br>±60.26   | 0.20   |
| Mean<br>± SD<br>(mins.) | Sensory | 305.066<br>±83.64 | 580.166<br>±111.45 | 0.0001 |

As table 4 shows duration of motor anesthesia in group-I and group-II were respectively 284.33±78.94 and 307.33±60.26 mins. P=0.20, so it is insignificant. While duration of sensory anesthesia in group-I and II were respectively 305.066±83.64 and 580.166±111.45 mins. P value=0.0001, which suggests duration of sensory blockade was significantly longer in buprenorphine group than group I.

**Table 5: Side effects.**

| Side effects           | Group I | Group II |
|------------------------|---------|----------|
|                        | No.     | No.      |
| Arterial Puncture      | -       | -        |
| Inadequate block       | 1       | -        |
| Failed block           | 1       | 1        |
| Bradycardia            | -       | 1        |
| Nausea and vomiting    | -       | 1        |
| Respiratory depression | -       | -        |

## DISCUSSION

Axillary brachial plexus is a simple, safe and easy technique. It provides anesthesia to the patients undergoing ambulatory upper extremity surgery. Regional anesthesia provides preemptive as well as postoperative analgesia. Adding opioids to the local

anesthetic drug in brachial plexus block improves quality and duration of block as well as duration of postoperative analgesia.

This randomized axillary block study was carried out in 60 patients scheduled for upper limb surgery. Both the groups had similar demographic and surgical profile. We used bupivacaine in control group (Group I) and bupivacaine with buprenorphine (3µg/kg) in the test group (Group II). In both the groups patients were of ASA grade-I and II.

Our study showed that addition of buprenorphine to bupivacaine for axillary block did not affected onset of motor or sensory anesthesia. This can be explained by core and mentle concept described by Winneet al.<sup>10</sup> Various studies reported about the existence of opioid receptors outside the central nervous system and described about peripheral action of opioids. Shaaban A Mousa reported that opioids containing immunocytes migrate to the inflamed sites where they replace β-endorphin which activates peripheral opioid receptors and produces analgesia.<sup>6</sup>

Mean duration of motor block was 284.333±78.94 mins in group-I while in group-II 307.333±60.26 mins. Mean duration of sensory block was 305.0667±83.64 mins in group-I while in group-II it was 580.1667±111.45 mins. It indicates that addition of buprenorphine to the local anesthetic in peripheral nerve block provides 2 fold increase in the duration of postoperative analgesia. J.E. Bazin, Massoni concluded that addition of an opioid to a local anesthetic mixture lengthens the duration of analgesia.<sup>11</sup> Present study also agree with the study concluded by viel EJ who inferred that the duration of analgesia was nearly twice with buprenorphine.<sup>9</sup> In study concluded by Candido KD and Winnie AP had shown that the duration of analgesia lasting 3 times longer with using buprenorphine than local anesthetic alone in peripheral nerve block.<sup>12</sup>

No significant change was observed in vital data like pulse rate, MAP, RR during perioperative period.

In this study, a neither allergic nor toxic reaction to local anesthetic or opioids was found in any patients. One patient in group-II had nausea and vomiting which was treated by inj. Ondansetron 4 mg, i.v. Two patients in group-I and one patient in group-II were supplemented with general anesthesia due to unsatisfactory effect of the block.

## CONCLUSIONS

Addition of buprenorphine (3 µg/kg) to bupivacaine mixture in peripheral nerve block not affected the onset time for motor as well as sensory block. Addition of buprenorphine to the local anesthetic in peripheral nerve block provides 2 fold increase in the duration of postoperative analgesia. Though buprenorphine is older drug but it is longer acting than newer drug like fentanyl,

Remifentanyl and gives good post operative analgesia so we have to take it again under consideration.

No significant complications of buprenorphine were found when given by peripheral route as compared to systemic route. Hence, buprenorphine significantly prolongs sensory block and lengthens the duration of analgesia without prolonging the duration of motor block.

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