Effect of Nalbuphine as an adjuvant to 0.5% Bupivacaine for supraclavicular brachial plexus block

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Abstract---BACKGROUND: Brachial plexus block is most common regional anaesthetic technique for upper arm and hand surgeries. Nalbuphine is a derivative of hydroxymorphine with mixed agonist, antagonist properties and is a strong analgesic. The present study was carried out to evaluate the effect of Nalbuphine added to 0.5% Bupivacaine for supraclavicular brachial plexus block. MATERIALS AND METHODS: 60 adults patients posted for forearm and hand surgeries under supraclavicular brachial plexus block were divided into two equal groups in a randomised double-blind manner. Gr I (n=30) received 29 ml 0.5% Bupivacaine + 10 mg Nalbuphine hydrochloride (1 ml). Gr II received 29 ml of 0.5% Bupivacaine + 1 ml Normal Saline (0.9%). Study drug was administered in supraclavicular brachial plexus block by B. Braun Stimuplex HNS12 peripheral nerve stimulator. Following parameters were studied. Onset time, duration of sensory and motor block, time to first analgesia use. Post operative analgesia was evaluated by visual analog scale (VAS) score, hemodynamic changes and side effects were recorded after block. RESULTS: Onset time was comparable in both the groups. Duration of sensory & motor block, time for first analgesic use and post operative
analgesia was significantly longer in Gr I than Gr II. Intra operative hemodynamic changes was comparable between two groups. CONCLUSION: Adding Nalbuphine to Bupivacaine for supraclavicular brachial plexus block increase the sensory and motor block duration without significant side effects.

**Keywords**—bupivacaine, nalbuphine hydrochloride, supraclavicular brachial plexus block, post op analgesia.

**Introduction**

Pain is an unpleasant sensory & emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain frequently hampers the implementation of day care surgical procedure inspite of use of various analgesic drugs & regimens. Post operative pain is the most unpleasant sensation experienced by patients undergoing surgery under general anaesthesia, hence perioperative pain management is the main aim of any anaesthetic procedure. Good post operative anaesthesia positively improves the surgical outcome. Out of various modalities of post operative pain relief regional blocks are used most frequently with commendable outcome. Brachial plexus block is most commonly used regional anaesthetic technique for surgeries of upperlimb. It is formed by the ventral rami of C5 to T1 sometimes with small contributions by C4 & T2. A variety of approaches of brachial plexus block have been described in the literature, however supraclavicular block is a consistent & easiest method of anaesthesia & post operative pain management. In supraclavicular approach, it blocks all the nerves of brachial plexus with equal potency because here brachial plexus trunks & cords are compactly arranged around subclavian artery, so small volumes of local anaesthetic solution produces rapid onset of reliable blockage. It provides good intraoperative anaesthesia and post operative analgesia, early ambulation and discharge from hospital(1). By brachial plexus block the complications involving general anaesthesia like airway manipulation and use of multiple drugs can be avoided.

Among various local anaesthetics available a suitable drug is chosen so that appropriate block will outlast majority of surgical procedures. Bupivacaine a long acting amide local anaesthetic is most commonly used for brachial plexus block. Local anaesthetic alone for brachial plexus block provides good operative conditions but have a limited duration of action. Hence various adjuvants such as Opioids(2), Clonidine(3), Neostigmine, Dexamethasone(4), Midazolam(5) and Magnesium(6) have been added to local anaesthetics in brachial plexus block to achieve intense and prolonged block and produce post op analgesia. Nalbuphine is a derivative of 14 – hydroxymorphine is an antagonist at mu receptors and agonist at kappa receptors with an analgesia potency equal to Morphine. Its antagonist properties is approximately 1/4th of Naloxone(7). However unlike Morphine it exhibits a ceiling effect on respiratory depression(8). Nalbuphine has the potential to enhance mu opioid based analgesic effect while simultaneously mitigating the mu opioid side effects(9). Nalbuphine is used as an adjuvant to local anaesthetic in neuraxial block to prolong the duration of block. The present study was conducted to evaluate the duration of analgesia by adding Nalbuphine
to Bupivacaine in patients posted for upper limb surgeries under supraclavicular brachial plexus block.

**Methods**

A prospective, randomised, double blind controlled study was carried out after taking approval from institutional ethical committee and informed consent from patients. Sixty adult patients of either sex, ASA Gr I & II between age groups of 18-60 yrs scheduled for elective forearm and hand surgeries in orthopaedics and plastic surgery department were enrolled for the study. Proper preoperative assessment was done on previous day of surgery. The nature, risk & safety of the procedure was explained and, informed consent obtained. During pre anaesthetic checkup all patients were advised to take TAB Alprazolam (0.5 mg) and TAB Ranitidine (150 mg) at bedtime and 6 hrs nil orally. They were randomly divided into two equal groups (n=30) according to computer generated random number. Gr I – Received 29 ml of 0.5% Bupivacaine with 1 ml (10 mg) of Nalbuphine. Gr II – Received 29 ml of 0.5% Bupivacaine 29 ml with 1 ml of 0.9% normal saline.

Study drug was prepared by another anaesthesiologist who was unaware about the study. On the day of surgery, the patients who were satisfying our criteria were included in the study group. On arrival in the operation theatre monitors were connected to record NIBP, ECG, pulse oximetry (Spo2) and heart rate (HR). Basal vital parameters were recorded. Intravenous line with a 18 G cannula was secured on healthy hand and crystalloid was infused. Patients were sedated with IV midazolam(0.05 mg/kg) before block was administered. No analgesic drugs were given during premedication. Patients lie down with a roll below the shoulder; head turned 45 degrees to contralateral side with adduction of ipsilateral arm. Supraclavicular block was performed under strict aseptic precautions. Subclavian artery pulsation was felt at a point 1 cm above mid point of clavicle. B. Braun Stimuplex HNS12 peripheral nerve stimulator was used for this purpose. After explaining the technique to the patient a mark was made at 1 cm above the mid clavicular point just lateral to subclavian pulsation. The 22 G 5 cm insulated Stimuplex HNS12 needle was used. The stimulation frequency was set at 1 Hz and the stimulating current was initially set to deliver 1.5 mA and then decreased gradually. The position of the needle is consider proper if with current output of < 0.5 mA motor response is elicited in forearm and hand. After negative aspiration for blood, total volume of study drug (30 ml) was injected.

The onset of sensory block was assessed by pin prick method using 25 G hypodermic needle in the appropriate area using a 3 point scale for pain (2 – sharp pain, 1 – blunt pain, 0 – no pain) in any dermatome (C5 – T1). The onset of sensory block was the time from completion of injection of study drug to first loss of pin prick sensation. Motor weakness was assessed by hand grip and movement at elbow, wrist and fingers using Modified Bromage Scale.

Gr 0 – Normal motor function.
Gr 1 – Able to raise the extended arm to 90 degrees.
Gr 2 – Unable to flex the elbow but able to move fingers.
Gr 3 – Complete motor block(10).
The onset time of motor block was from completion of injection to reduction of muscle force to Gr 2. The duration of motor block is from onset of block to complete recovery of muscle power. Every patients were assessed for onset of sensory and motor block at every 5 minutes interval till desired surgical anaesthesia level achieved. Inadequate block where patients complained of pain during surgery or required addition of intravenous anaesthesia were excluded from the study group. All the patients were given inj. Midazolam 0.03mg/kg IV for intraoperative sedation. Intraoperative vital parameters like NIBP, HR, SPO2 were recorded every 5 minutes interval till the completion of surgeries and then every 30 minutes interval till rescue analgesia is required. Patients were also observed for any untoward effects like hypotension, bradycardia, fall of SPO2, nausea, vomiting, pruritus etc. The duration of post op analgesia was assessed by using 10 point VAS(Visual Analog Scale) ; where 0 – no pain and 10 – worst pain. Inj. Butorphanol 1 mg was given IV as rescue analgesia where VAS > 4.

**Statistical Analysis**

Statistical analysis was performed using the SPSS software. Data presented as mean and standard deviation (SD) or number and percentage. The t – test was used to examine the differences between mean and SD. Statistical significance was accepted for a P value of < 0.05.

**Results**

A total of 60 patients of ASA Grade I & II of both sex, aged between 18 – 60 years undergoing forearm and hand surgery in orthopaedic and plastic surgery OT of MKCG medical college & hospital who satisfied the inclusion criteria had been enrolled in the study. They were randomly allocated into two groups of 30 patients each. Demographic data including age, sex, weight, ASA classification and duration of surgery were comparable between 2 groups.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>GROUP I ( N = 30)</th>
<th>GROUP II (N = 30)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE IN YRS</td>
<td>36.7 +/- 8.64</td>
<td>38.10 +/- 7.87</td>
<td>0.623</td>
</tr>
<tr>
<td>BODY WIGHT IN KG</td>
<td>54.85 +/- 8.54</td>
<td>52.60 +/- 11.90</td>
<td>0.0791</td>
</tr>
<tr>
<td>MALE : FEMALE</td>
<td>20 : 10</td>
<td>18 : 12</td>
<td></td>
</tr>
<tr>
<td>ASA GRADE I / II</td>
<td>14 : 16</td>
<td>22 : 8</td>
<td></td>
</tr>
<tr>
<td>MEAN DURATION OF SURGERY</td>
<td>115.75 +/- 25.67</td>
<td>118.25 +/- 23.57</td>
<td>0.647</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>GROUP I ( N= 30)</th>
<th>GROUP II (N=30)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIME FOR SENSORY BLOCK IN MINUTES</td>
<td>11.57 +/- 2.81</td>
<td>12.91 +/- 3.69</td>
<td>0.148</td>
</tr>
</tbody>
</table>
Regarding onset of sensory and motor block results showed that there is no statistical significant difference on onset time of block between the two groups. P VALUE > 0.05; there was no significant difference in onset of sensory & motor block in both the groups.

Table 3
Duration of Block

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>GROUP I (NALBUPHINE)</th>
<th>GROUP II (CONTROL)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>DURATION OF BLOCK IN HRS</td>
<td>5.30 +/- 1.40</td>
<td>2.5 +/- 0.77</td>
<td>0.0019</td>
</tr>
<tr>
<td>TIME FOR RESCUE ANALGESIA</td>
<td>5.61 +/- 1.49</td>
<td>2.78 +/- 0.75</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

Total duration of block was prolonged in Nalbuphine group. Time required for rescue analgesia was significantly prolonged in Nalbuphine group. The duration of sensory block and rescue analgesia time was prolonged in Gr I as compared to Gr II. P VALUE < 0.001.
Table 4
Perioperative Hemodynamic Variables

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>GROUP I (N=30)</th>
<th>GROUP II (N=30)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse Rate/Min</td>
<td>88.15 +/- 5.40</td>
<td>85.70 +/- 6.24</td>
<td>0.4468</td>
</tr>
<tr>
<td>SBP in MMHG</td>
<td>123.40 +/- 7.11</td>
<td>120.70 +/- 7.98</td>
<td>0.5381</td>
</tr>
<tr>
<td>DBP in MMHG</td>
<td>78.30 +/- 7.26</td>
<td>86.10 +/- 6.20</td>
<td>0.4004</td>
</tr>
<tr>
<td>SPO2</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

P VALUE > 0.05 indicate no significant change in perioperative hemodynamic variable in both nalbuphine & control group. The perioperative vital parameters like HR, systolic and diastolic blood pressure & SPO2 are comparable between two groups.

**Discussions**

Day care surgery has proven to be best method as it avoids prolonged hospital stay & indirectly burden on health care resources. By regional technique we can also avoid airway manipulation, delayed recovery and discharge from hospital rather post operative analgesia can be better achieved. The advantages of supraclavicular brachial plexus block is, as the nerves are here compactly arranged, injecting local anaesthetics at supraclavicular region cause rapid onset, predictable and dense anaesthesia along with high success rate(11). Different adjuvants like Dexmedetomidine, Clonidine, Midazolam and different opioids added to local anaesthetics have been tried for better and prolonged block. Nalbuphine is a mixed Kappa agonist and mu antagonist opioid and its affinity to Kappa – opioid receptors results in analgesia, sedation & cardiovascular stability with minimal respiratory depression. It potentiate local anaesthetic action
through central opioid receptors mediated analgesia by peripheral uptake of Nalbuphine to systemic circulation.

Young et al demonstrated that opioid receptors and various macromolecules in the nerve undergo axonal flow(14). Opioid penetrate the nerve membrane and act at dorsal horn. Laurdren speculated that these receptors circulate endorphin in addition to exogenous opioids which act directly on peripheral nervous system(15). In the present study we compared the effect of nalbuphine hydrochloride(10 mg) 1 ml added to 29 ml of 0.5% bupivacaine and 1 ml of normal saline added to 29 ml of 0.5% Bupivacaine as control group on supraclavicular brachial plexus block. The different parameters studied are onset and duration of sensory & motor block, post op analgesia and hemodynamic changes. In our study there was a significant increase in the duration of analgesia in patients who received Nalbuphine as an adjuvant ( 5.30 +/- 1.4 hr) as compared to (2.5 +/- 0.11 hr) in control group. The prolongation in block duration may be due to synergistic action of Nalbuphine with Bupivacaine.

You s set & Elzayyat compared the effect of Nalbuphine with Tramadol as adjuvant of Lidocaine in intravenous regional anaesthesia & concluded that post operative duration of analgesia is prolonged with Nalbuphine than Tramadol(16). Abdel hag & Elramely(17) used 20 mg Nalbuphine as adjuvant to 25 ml of 0.5% Bupivacaine for supraclavicular brachial plexus block for upper arm surgeries & found Nalbuphine prolongs duration of sensory & motor block and post op analgesia. In our study we found the same result with reduced dose of Nalbuphine 10mg. In our study the benefits of Nalbuphine were not associated with any hemodynamics changes or adverse event like pruritus, nausea, vomiting & respiratory depression as Nalbuphine is a agonist at K receptors & antagonist to u receptors. Patients were comfortable due to painless performance and no post op pain or side effects.

Conclusion

Nalbuphine 10 mg as an adjuvant to 0.5% Bupivacaine for supraclavicular brachial plexus block in patients undergoing various fore arm & hand surgeries is associated with prolonged duration of sensory, motor block & post operative analgesia. There was no remarkable hemodynamics changes or adverse effects. Nalbuphine may be considered as one more addition to expand the list of adjuvants to local anaesthetics for central & peripheral nerve blocks. However further studies are awaited to confirm my study.

References


