Efficacy of Butorphanol and Tramadol as an Adjuvant to Levobupivacaine for Postoperative Analgesia in Brachial Plexus Block: A Randomized Double-Blind Study

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Abstract

Background: SuprACLavicular brachial plexus block has evolved as a safe alternative to general anaesthesia with good postoperative analgesia. In an attempt to hasten the onset of block and increase the duration of postoperative analgesia, various adjuvant drugs are used along with local anesthetic agents.

Aim: The present study was undertaken to assess the analgesic efficacy of butorphanol (2 mg) and tramadol (100 mg) as an adjuvant to levobupivacaine in suprACLavicular brachial plexus block during perioperative period.

Study Design: This was a prospective, randomized, double blind study done on 100 adult patients of ASA I-III aged between 18-65 years and scheduled for various upper limb surgeries below the level of elbow.

Materials and Methodology: Patients were allocated by computer generated random draw into two groups of 50 each and were administered the study drugs under ultrasonographic guidance. Both groups received 22 ml of the study drug (Group B 20 ml 0.5% levobupivacaine + Butorphanol 2 mg and Group T 0.5% levobupivacaine + Tramadol 100 mg). Patients were assessed for duration of postoperative analgesia, onset & duration of sensory as well as motor blockade and occurrence of any side effects.

Results: Duration of postoperative analgesia was significantly elevated in group B (683±88.58 min.), as compared to group T (483.2±45.24 Min.) with p< 0.001. Onset of sensory and motor blockade was comparable among both groups (p> 0.05). Duration of sensory and motor block in group B was significantly longer compared to group T (p< 0.001). Hemodynamics were stable and side effects were minimal in both the groups.

Conclusion: Butorphanol 2 mg when added to 20 ml 0.5% levobupivacaine in brachial plexus block, significantly prolongs the duration of postoperative analgesia, sensory and motor block as compared to addition of 100 mg tramadol, with minimal side effects and hemodynamic changes. However, these adjuvants shorten the onset times of sensory and motor block to a similar extent.

Keywords: Brachial plexus block, Levobupivacaine, Butorphanol, Tramadol, Analgesia.
humerus to hand, because of the anatomical ease of blocking nerve roots at this level. Ultrasound guided peripheral nerve block is a recent technique for accurate and improved quality of nerve block thereby reducing block failures and avoids procedure related complications like intraneural, intrathecal and intravascular injections as well as Local Anaesthetic Systemic Toxicity (LAST) [2].

Even though regional anesthesia offers excellent postoperative analgesia, the duration of a single shot peripheral nerve block is limited. Adjuvants are pharmacological agents that are added to local anesthetics to enhance the potency and duration while reducing the total dose of local anesthetic needed. Many drugs like morphine, neostigmine, tramadol, fentanyl, hyaluronidase, midazolam, dexmedetomidine, clonidine, dexamethasone, butorphanol, sodium bicarbonate, nalbuphine etc. have been added to local anesthetics to improve the quality of block, duration of action and postoperative analgesia [3].

Levobupivacaine a S-enantiomer of bupivacaine which belongs to an amino-amide group, has favorable clinical profile and margin of safety with respect to both cardiovascular system and central nervous system effects compared with racemic bupivacaine [4]. Butorphanol, an efficacious synthetic agonist-antagonist opioid has been shown to have a minimal side effect profile among opioids [5]. Tramadol has both opioid and non-opioid analgesic actions. It has low potential for the development of tolerance, dependence, and abuse and produces analgesia without ventilatory depression [6]. There is paucity of literature comparing duration of postoperative analgesia of butorphanol and tramadol as adjuvants to levobupivacaine in ultrasound guided supraclavicular brachial plexus block. Hence this study was planned to evaluate the effectiveness of these adjuvants to the study drug, for postoperative analgesia by the aforementioned interventional technique.

**Materials and methods**

This prospective randomized double-blind study was conducted in Department of Anaesthesiology and Pain Management over a period of one year, after approval from Institutional Ethics Committee and Institutional Scientific Committee. This study was registered with Clinical Trials Registry of India (CTRI NO- CTRI/2022/04/041666). After obtaining written informed consent a total of 102 patients of American Society of Anaesthesiologist- physical status (ASA-PS) I, II and III in the age group 18-65 years posted for elective mid arm and below elbow surgery were included in the study. Patients not willing to be part of the study, those having allergy to study drugs, bleeding disorder, severe respiratory, renal and liver disorder, neurological deficit involving brachial plexus, local infection at the injection site, pregnant women and morbidly obese (BMI >40 kg/m²) were excluded from the study.

The patients were divided by computer generated random draw by an anaesthesiologist who was involved only in preparation of the study drug, for the two groups B and T of 50 each. Group B received 20 ml of 0.5% levobupivacaine + 2 mg butorphanol whereas Group T received 20 ml of 0.5% levobupivacaine + 100 mg tramadol (total volume 22 ml). The anaesthesiologist involved in administering the study drug and postoperative assessment was not involved in either allocation of study groups or preparation of study drug, to ensure double blinding of the study.

A detailed preanaesthetic check-up was performed on the day prior to the surgery. All patients were kept fasting overnight. Patients were explained in the language they could comprehend about the brachial plexus block and linear visual analog score (VAS) scale using a 10 cm line, where 0 denoted “no pain” while 10 “worst pain imaginable”.

After shifting the patient to the operation theater baseline vital parameters [heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), SpO₂, respiratory rate (RR)] were recorded and were monitored continuously till the completion of surgery. Intravenous line was secured by inserting 18 G intravenous cannula and ringer lactate at the rate of 10 ml/kg/h was infused. Patients were placed in supine position with the head turned laterally away from the side of the nerve block and the arms were placed along the side of the body. After explaining the procedure to the...
patient, under strict aseptic precautions ultrasound guided supravacullar brachial plexus block was administered (Mindray Diagnostic Ultrasound System Model M7, Shenzhen Biomedical electronics, China). The brachial plexus was visualized using an 8-13 Hz linear array probe placed in the transverse plane in the supravacular region at the midpoint of the clavicle. The subclavian artery was seen as a circular, pulsating, hypoechoic shadow which was surrounded by multiple hypoechoic grapes like clusters with hyperechoic margins: the trunks of the brachial plexus. The study drug was administered using a 22G hypodermic needle advanced in plane in a lateral to medial direction. All vital parameters were recorded after administration of drug at every 5 min. interval up to 30 min., every 15 min. interval up to 60 min., every hour up to 4 hours and then every 4 hours up to 24 hours.

The primary outcome of this study was to determine duration of postoperative analgesia. The onset and duration of sensorimotor block and any adverse effects - nausea, vomiting, pruritis, respiratory depression, or allergic reactions, were recorded as secondary outcomes.

After supravacular block administration, sensory and motor block assessment was done using Hollmen and Modified Bromage scale respectively.

Onset time for sensory block was defined as the time interval between the end of local anesthetic administration and complete sensory block (score 4 for all nerves), and was assessed at 5-minute intervals.

### Results

The one hundred patients analyzed for the study were comparable with respect to demographic profile (age, sex, weight, ASA grading and duration of surgery) (Table 1) and baseline vital parameters (Table 2).

The mean time of onset of sensory block in group B was 11.7±3.02 min and in group T was 11.48±2.85 min. The mean time of onset of motor block in group B was 16.4±3.3 min and in group T was 13.8±3.02 min. This difference in mean onset time of sensory and motor block between the two groups was statistically not significant (p>0.05)(Table 3).
The mean duration of sensory block in group B was 532.8 ± 81.97 min and in group T was 342.6±36.19 min. The duration of sensory blockade was prolonged in group B and this difference between the two groups was highly significant (p<0.001). The duration of motor blockade in group B was 411 ± 67.8 min and in group T was 277.6 ± 31.85 min. The duration of motor blockade was also prolonged in group B and this difference in duration between the two groups was highly significant (p<0.001) (Table 3).

Mean duration of analgesia in group B was 683.00 ± 88.58 min and in group T was 483.2 ± 45.24 min. Duration of analgesia was prolonged in group B and this difference was statistically highly significant (p<0.001) (Table 3) (Graph 1).

In our study we observed nausea in two patients (4%) in group B and in one patient (2%) in group T.

**Discussion**

Supraclavicular approach to brachial plexus block is routinely used for surgeries of upper limb from mid humerus to hand which is safe and easy to administer. The most popular local anaesthetic (LA) used for peripheral nerve blocks is bupivacaine. Levobupivacaine, the S-enantiomer of bupivacaine, was employed in this study instead of bupivacaine due to its equal efficacy, improved CVS stability, and safer neurological profile due to its faster protein binding rate [8]. Additionally, LA combinations have been utilized to speed up the onset of sensory and motor block. In order to reduce the dosage of each agent, and to improve the quality and duration of block, boost the analgesic impact, and decrease the need for additional analgesics, certain drugs such as morphine, neostigmine, tramadol, fentanyl, midazolam, dexmedetomidine, clonidine, dexamethasone, butorphanol, sodium bicarbonate, nalbuphine etc. have been used in literature as adjuvants to LA [3]. These adjuvant drugs can have dose-dependent side effects. α-2-adrenergic agonists such as clonidine and dexmedetomidine can cause hypotension, bradycardia, sedation [9]. Dexamethasone can cause peripheral neurotoxicity and an increase in the postoperative glucose concentration subsequent to either perineural or i.v. administration [10]. Midazolam can also cause neurotoxicity [11]. Opioids such as buprenorphine, fentanyl, morphine are associated with nausea, vomiting, pruritis, respiratory depression. Adverse events like hallucination, nausea and drowsiness may be seen with ketamine [12].

In this study we used inj. butorphanol and inj. tramadol as an adjuvant to levobupivacaine in supraclavicular brachial plexus block. Butorphanol, a mixed agonist-antagonist opioid has been proven to have minimal side effect profile among opioids. Tramadol has both opioid and non-opioid analgesic actions. It has low potential for the development of tolerance, dependence, and abuse and produces analgesia without ventilatory depression. The duration of blockade and postoperative analgesia in supraclavicular brachial plexus block is prolonged when butorphanol (2 mg) is added to levobupivacaine without compromising hemodynamic parameters or causing any notable adverse medication responses. It is postulated that primary afferent tissues (dorsal roots) contain opioid receptors. Opioids diffuse out from the brachial plexus sheath and bind with opioid receptors at the dorsal horn and from there get transported into substantia gelatinosa through centripetal axonal transport, thereby causing a systemic analgesic effect. Also, it is speculated that during axonal transport these opioid receptors release and circulate endogenous endorphins, which further augment the duration of analgesia [10, 13].

In brachial plexus block, onset time with levobupivacaine alone usually varies from 15 to 20 minutes [14], but in this study, the onset times for groups B and T were 11.7±3.02 minutes and 11.48 ± 2.85 minutes, respectively which may be because of addition of adjuvants to levobupivacaine (Table 3). Similar to our study, previous research has found that butorphanol 2 mg and tramadol 100mg when added to levobupivacaine for supraclavicular brachial plexus block shorten time of onset of sensory and motor block similarly but butorphanol prolongs sensory and motor blockade more significantly [7, 15, 16, 17].

In our study, mean duration of analgesia in group B was 683.00 ± 88.58 min and in group T was 483.2 ± 45.2 min. Duration of analgesia was prolonged in group B as compared to group T and this difference in duration of postoperative analgesia was statistically highly significant (p<0.001) (Table 3, Graph 1). Results of our study were in concordance with other studies where they concluded that butorphanol 2mg when added to local anaesthetic for brachial plexus block prolongs duration of post-operative analgesia.

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**Table 3 - Primary and secondary outcomes**

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Group B</th>
<th>Group T</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean onset of sensory block (min)</td>
<td>11.7 ± 3.02</td>
<td>11.48 ± 2.85</td>
<td>0.71 NS</td>
</tr>
<tr>
<td>Mean onset of motor block (min)</td>
<td>16.4 ± 3.3</td>
<td>15.38 ± 3.02</td>
<td>0.11 NS</td>
</tr>
<tr>
<td>Mean duration of sensory block (min)</td>
<td>532.8 ± 81.97</td>
<td>342.6±36.19</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>Mean duration of motor block (min)</td>
<td>411 ± 67.8</td>
<td>277.6±31.85</td>
<td>&lt;0.001 HS</td>
</tr>
<tr>
<td>Mean Duration of analgesia (min)</td>
<td>683 ± 88.58</td>
<td>483.2 ± 45.24</td>
<td>&lt;0.001 HS</td>
</tr>
</tbody>
</table>

**Graph 1: Mean duration of analgesia**

[Graph depicting mean duration of analgesia]
significantly more than that of tramadol 100 mg [7, 18, 19, 20, 21].

In our study, there were no significant changes in the hemodynamic parameters in either group.

Nausea was noted in two patients in group B and in one patient in group T (Table 4). Nausea is a subjective, extremely unpleasant sensation. Although nausea and vomiting can occur separately and have separate and distinct mechanisms of development, nausea often precedes vomiting. Three key mechanisms most widely thought to cause opioid induced nausea and vomiting (OINV) are stimulation of the chemoreceptor trigger zone (CTZ), increased vestibular sensitivity, and delayed gastric emptying.

As we performed ultrasound-guided supraclavicular brachial plexus block it resulted in more accurate drug deposition, reduced volume of local anaesthetic and thereby minimal side effects. No significant differences regarding intraoperative adverse effects and complications were found in the two groups. This insignificant difference is in line with previous studies [7, 18].

## Conclusion

We concluded that addition of 2 mg of butorphanol significantly prolongs the duration of postoperative analgesia, sensory and motor block as compared to 100 mg tramadol with minimal side effects and hemodynamic changes.

### References

[16] Vinod CN, Talikoti DG. Comparison of Butorphanol and Buprenorphine as an Adjuvant to Local Anesthesia in Supraclavicular Brachial Plexus Block for Postoperative Analgesia. Journal of Evolution of Medical and Dental Sciences 2014;3:4287-93

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**Table 4- Side effects**

<table>
<thead>
<tr>
<th>Side effects</th>
<th>No. of patients in group B</th>
<th>No. of patients in group T</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>2 (4%)</td>
<td>1(2%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Allergic reactions</td>
<td>0</td>
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</table>
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Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.

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