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Comparative Evaluation of Nalbuphine and Tramadol as an Adjuvant to 0.5% Bupivacaine in Supraclavicular Brachial Plexus Block

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Abstract

Background: Brachial plexus block is a reliable, regional anesthetic technique for upper arm surgeries. Opioid agonist-antagonists are used as adjuvant to enhance the analgesia of bupivacaine. The present study was aimed to compare the analgesic efficacy and safety of nalbuphine and tramadol as an adjuvant to 0.5% bupivacaine for brachial plexus block. *Materials and Methods:* Thirty adult patients of ASA I and II of both genders were randomized into two Groups of fifteen patients, Group BT receive 28 ml of 0.5% bupivacaine with 2 ml of tramadol and Group BN receive 28 ml of 0.5% bupivacaine with 2 ml of nalbuphine 20 mg for supraclavicular brachial plexus block. Patients were observed for onset and duration of sensory and motor block with duration of pain relief as primary end points while occurrence of any adverse effect due to technique or nalbuphine was noted as secondary outcome. *Results:* In Group BN, there was a statistically significant shorter time to onset of sensory blockade (10.46 ± 1.5 min vs 13.66 ± 2.5 min, $p < 0.001$), shorter onset time to achieve motor block (14.4 ± 2.5 min vs. 18.46 ± 3.5 min, $p < 0.001$), longer duration of motor block (291.4 min vs 363.07 min, $p < 0.001$), and prolonged analgesia (456 min vs 409.13 min, $p = 0.003$). No significant side effects were seen in any of the groups. *Conclusion:* Addition of nalbuphine to 0.5% bupivacaine in supraclavicular brachial plexus block significantly hastens the onset, and prolongs the duration of sensorimotor blockade and analgesia when compared with tramadol as an additive. Both the drugs were comparable in terms of safety.

Keywords: Brachial plexus block; Bupivacaine; Nalbuphine; Tramadol; Additive.

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Introduction

The supraclavicular block is often called the "spinal anesthesia of the upper extremity" because of its ubiquitous application for upper extremity surgery. It is a reliable, alternative to general anesthesia for certain group of patients as it is devoid of undesired effects of general anesthesia and stress of laryngoscopy. The post-operative period is also free from pain, nausea, vomiting, and respiratory depression. The supraclavicular approach is chosen for brachial plexus block as here it is enclosed in a fascial sheath that extends from neck to the axilla.[1] The success of brachial plexus block relies on nerve localization, needle placement, and deposition of local anesthetic solution at right place by a single injection of local anesthetic.[1] Nerve stimulatorare

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better than blind technique as they not only increase the accuracy but also prevent several complication that may arise due to blind technique. It also minimizes the local anesthetic volume, thereby reducing the incidences of their systemic toxicity.[2,3] Bupivacaine relieves pain by blocking the transmission of pain signals to the dorsal horn, but it has definite risks of systemic toxicity, especially with brachial plexus block. Various adjuvants like opioids, clonidine, dexmeditomedine are added in peripheral nerve blocks to increase speed of onset, duration of action, improve quality of the block and to reduce toxicity of local anesthetics.[4] However, they are associated with side effects like heavy sedation and respiratory depression. Therefore, there is always look out for drugs with minimal side effects. Opioids have an anti-nociceptive effect at the central or spinal cord levels. Stimulation of opioid receptors on neurons of central nervous systems leads to the inhibition of neuronal serotonin uptake which leads to augmentation of spinal inhibitory pain pathways; however, it is still unclear whether functional opioid receptors exist in peripheral tissue.[5] Many opioids such as tramadol and fentanyl have been added as adjuvants to local anesthetics by different routes, including brachial plexus block, to enhance the analgesic efficacy. Effects of opioids are either by their action on opioid receptors or by systemic absorption. Tramadol is an analgesic with μ mixed opioid and non-opioid activity. It inhibits the reuptake of norepinephrine (NE) and serotonin from the nerve endings and potentiates the effects of local anesthetics when mixed together in peripheral regional nerve block. It has less respiratory depressant effect due to weak μ receptor affinity.[6]

Nalbuphine hydrochloride, a potent analgesic,[7] acts as a Kappa agonist and partial mu antagonist.[7,8,10] Its affinity to κ-opioid receptors results in sedation, analgesia, and cardiovascular stability with minimal respiratory depression.[7,10]

It may potentiate local anesthetic action through central opioid receptor-mediated analgesia by peripheral uptake of nalbuphine to systemic circulation. It is widely studied as an adjuvant to local anesthetics in central neuraxial techniques by epidural, caudal, and intrathecal routes.[11] However, after research in literature, we did not find much published data studying the effect of nalbuphine as an adjuvant to local anesthetics in peripheral nerve blocks however, we are commonly using tramadol as an adjuvant to local anesthetic in our institute.

Hence, the present study was undertaken to compare the clinical efficacy and safety of tramadol versus nalbuphine as an adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block. The primary aim of this study was to compare tramadol versus nalbuphine as an adjuvant to 0.5% bupivacaine in supraclavicular brachial plexus blocks in terms of onset of block, duration of sensory and motor blockade and post-operative duration of analgesia and secondary aim is to compare safety of the two drugs in the form of side effect profile.

Materials and Methods

After approval of the Institutional Ethics Committee and obtaining written informed consent from each patient, thirty patients of American Society of Anesthesiologists (ASA) physical status I to II of both gender, aged *18–60 years*, scheduled for elective elbow, forearm and hand surgeries in orthopedic operation theatres, were enrolled for this prospective, randomized comparative control study.

Patients with clinically significant coagulopathy, infection at the injection site, allergy to local anesthetics, pre-existing neuromuscular diseases, severe cardiovascular or pulmonary disease, renal or hepatic disorder, refusal to technique, unco-operative or failure of block were excluded from the study. Patients on any opioids or any sedative medications in the week prior to the surgery were also excluded from the study. Visual analog scale (VAS) was explained to all patients where 0 corresponds to no pain and 10 indicates the worst unbearable pain.

Patients were randomized according to computer-generated random number table into two equal groups of fi fteen patients each, Group BT (Bupivacaine with tramadol) and Group BN (Bupivacaine with nalbuphine). Patients of Group BT received 28 ml of 0.5% bupivacaine with 2 ml (100 mg) of tramadol and patients of Group BN received 28 ml of 0.5% bupivacaine with 2 ml (20 mg) of nalbuphine for brachial plexus blockade by supraclavicular approach.

The study drug solutions were in similar volume of 30 ml, to maintain the blindness of study and were prepared by an anesthetist who was not involved for data collection of the patients. The anesthetist performing the block was also blinded to the study groups, and all observations were done by the same investigator.

All patients were admitted before the day of surgery, and fasting of *8 hours* was ensured. On arrival in the operation theatre, intravenous

access was established and lactated ringer lactate solution was infused at the rate of *6–8 ml/kg* and monitors for non-invasive blood pressure, heart rate, electrocardiogram (ECG), and pulse oximetry (SpO_2) were commenced to monitor the peri-operative vital parameters of patients. Patients lie down supine with head turned *45°* to the contralateral side with adduction of ipsilateral arm. A small bolster was placed between shoulder blades to make the plexus taut. The supraclavicular brachial plexus block was performed using a Vygon nerve stimulator with *22 g, 5 cm* insulated needle for precise location of brachial plexus. Under all aseptic precautions, a skin wheal was raised in the supraclavicular region, *1 cm* above the medial two third and the lateral one third of the clavicle. Subclavian artery is usually palpable on this site. Nerve stimulator frequency was set at *2 Hz* and intensity of stimulating current was initially set to deliver *1 mA* for *0.1 ms*. Insulated needle was inserted through the skin wheal in a posterior, caudal and medial direction until a distal motor response was elicited. As the nerve was approached, movement of the wrist or fingers were identified and the current was gradually reduced to *0.5 mA*. Position of needle was considered acceptable when an output current *0.5 mA* elicited a distal motor response. At this point after negative aspiration for blood, a mixture of local anesthetic and adjuvant as per the group allotted was given. All patients were given supplemental oxygen using ventimask. The onset of sensory block was assessed by pinprick method. The onset time of sensory block was the time from completion of the injection to first loss of pinprick sensation.

Motor weakness was assessed by hand grip and movement at the elbow, wrist and fingers, using a modified Bromage scale (Grade 0 - normal motor function, able to raise the extended arm to *90°*; Grade 1 - able to flex the elbow and move the fingers but unable to raise the extended arm; Grade 2 - unable to flex the elbow but able to move the fingers; Grade 3 - complete motor block). The onset time of motor block was the time from completion of the injection to reduction of muscle force to Grade 2. Motor block was also assessed by thumb abduction (radial nerve), thumb adduction (ulnar nerve), and thumb opposition (median nerve). Duration of motor block was taken from onset of motor block to complete recovery of full muscle power and was determined by asking the patients to note the time when they could first move their fingers of blocked limb. Patients were assessed for onset of sensory and motor blockade at every *2 min* interval till desired surgical anesthesia achieved with time *0 min* being the time of completion of the injection.

Intra-operative vital parameters of blood pressure, heart rate, respiratory rate, and peripheral oxygen saturation were monitored initially at *5 min* interval until *15 min* and then at *15 min* interval until completion of surgery. The quality of analgesia was assessed every hour post-operatively for *24 hours* in the recovery room and in surgical ward by attending nurse using VAS scale (1–10): zero was considered as no pain, 1–3 as mild pain, 4–6 as moderate pain, and 7–10 as severe pain. At the score of 4, nursing staff was directed to administer injection diclofenac sodium *75 mg* intramuscularly. Duration of analgesia was calculated from the time of local anesthetic injection to the time of first analgesic requirement. All patients were observed for any side effects such as nausea, vomiting, bradycardia and hypotension and complications of supraclavicular block like pneumothorax, hematoma, Local anesthesia toxicity, and post block neuropathy in the intra and post-operative periods and treated accordingly.

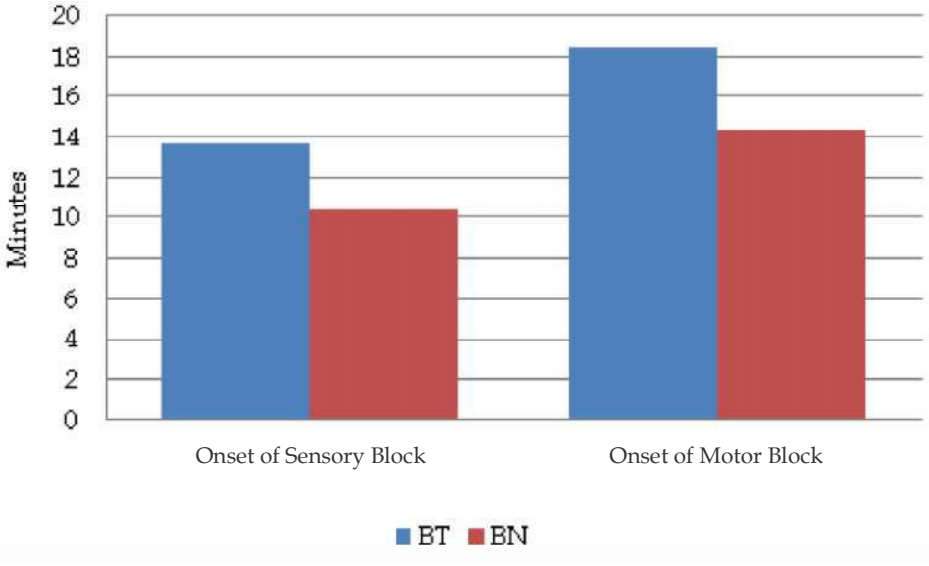
Results

Patients of both groups were comparable with respect to the demographic profile for age, sex distribution, ASA physical status. The baseline vital parameters of heart rate, systemic blood pressure, and oxygen saturation were comparable between the groups. Intra-operatively, hemodynamic changes did not reveal any significant difference between the groups and all patients remained hemodynamically stable throughout the surgery. Onset time of sensory block (*10.46 ± 1.5 min* vs. *13.66 ± 2.5 min*) and motor block (*14.4 ± 2.5 min* vs. *18.46 ± 3.5 min*) in Group BN was significantly faster than Group BT ($p < 0.001$), showed as in (**Table 1**), along with (**Graphics 1** and **2**).

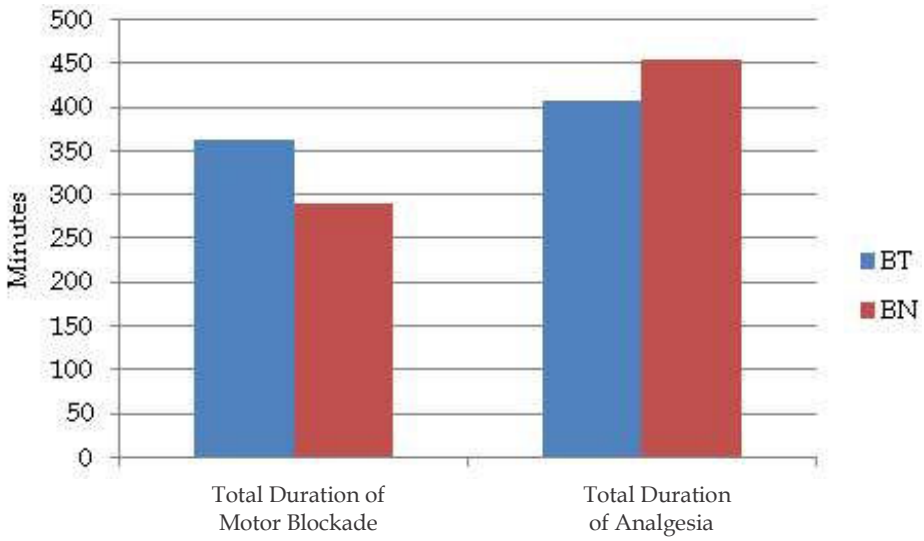
Table 1:

	Onset of sensory blockade	Onset of motor blockade
Group BT	13.66 +/- 2.5	18.46 +/- 3.5
Group BN	10.46 +/- 1.5	14.4 +/- 2.5
	Total duration of motor blockade	**Total duration of analgesia**
Group BT	*363.07 min/6.05 hrs*	*409.13 min/6.8 hrs*
Group BN	*291.4 min/4.8 hrs*	*456.00 min/7.6 hrs*

The mean duration of motor block was *291.4 min* in patients of Group BN when compared to Group BT (*363.07 min*) and the difference was statistically



Graph 1:



Graph 2:

significant ($p < 0.001$). The duration of analgesia in patients of Group BN was *456.00 min* and in patients of Group BT was *409.13 min* with p – value = 0.003. No side effect was seen in either Group.

Discussion

Brachial plexus blockade is commonly performed regional anesthetic technique for forearm and hand surgeries, and its blockage provides good surgical anesthesia. There are several advantages of regional anesthesia over general anesthesia in terms of safety, effective pain relief, and early discharge from the recovery room. However, additional analgesics are required for relieving the post-operative pain,[12,13,14,15] as the duration of action of currently available Local anesthetic agent is short. Increasing the dose of Local anesthetic agents may prolong the Duration of action[16] but may also increase the risk of LA systemic toxicity.[17]

Different opioids have been added to local anesthetic to improve the quality and duration

of post-operative analgesia of peripheral nerve blocks.[18] Many previous studies have attempted to determine whether the addition of opioid to local anesthetics would improve the clinical efficacy of peripheral nerve blocks and demonstrated that different types of opioids act well on peripheral nerve through stimulation of opioid receptor, but they were associated with unacceptable adverse effects. Tramadol and fentanyl were commonly used as adjuvant to local anesthetic drug in brachial plexus block.[19] Systemic review of various adjuvants for brachial plexus block suggested that the nalbuphine appeared to possess greater analgesic efficacy with minimal adverse effects.

Nalbuphine hydrochloride, a potent analgesic,[9] acts as a Kappa agonist and partial mu antagonist.[9,10,11] Its affinity to κ-opioid receptors results in sedation, analgesia, and cardiovascular stability with minimal respiratory depression.[9,10]

Tramadol is an analgesic with μ mixed opioid and non-opioid activity. It inhibits the reuptake of norepinephrine (NE) and serotonin from the nerve endings and potentiates the effects of local anesthetics when mixed together in peripheral regional nerve block. It has less respiratory depressant effect due to weak μ receptor affinity.[6]

Youssef and ElZayyat[20] compared the effect of nalbuphine with tramadol as adjuvants to lidocaine in intravenous regional anesthesia and concluded that both nalbuphine and tramadol were comparable, but nalbuphine was more effective than tramadol for prolonging the duration of post-operative analgesia.

Abdelhaq and Elramely[21] also used *20 mg* nalbuphine as adjuvant to *25 ml* of 0.5% bupivacaine for supraclavicular brachial plexus block for upper arm surgeries and concluded that nalbuphine has significantly increased the duration of both sensory and motor block along with prolonged post-operative analgesia.

In the present study, we observed the statistically significant enhanced onset of action, enhanced duration of motor block along with duration of analgesia with addition of nalbuphine to 0.5% bupivacaine as compared to tramadol in brachial plexus block. This prolongation of anesthetic effect and analgesia could be secondary to the stimulation of kappa receptors by nalbuphine, which inhibits release of neurotransmitters for pain such as substance P. The benefits of nalbuphine were not associated with any hemodynamic variability or any adverse event.

Conclusion

Nalbuphine is superior to tramadol in terms of onset of action, duration of motor blockade and post-operative duration of analgesia when added as an additive to bupivacaine in supraclavicular brachial plexus block.

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Conflicts of interest: There are no conflicts of interest.

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