International Journal of Medical Anesthesiology

E-ISSN: 2664-3774
P-ISSN: 2664-3766
www.anesthesiologypaper.com
IJMA 2023; 6(3): 95-99
Received: 12-05-2023
Accepted: 16-06-2023

Dr. Zareen Fatima
Post Graduate Junior Resident 3 rd year, Department of Anesthesia, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India

Dr. Ruchira Sarkar
Post Graduate Junior Resident 3 rd year, Department of Anesthesia, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India

Dr. Neeraj
Post Graduate Junior Resident 3 rd year, Department of Anesthesia, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India

Dr. Vishal Arora
Professor, HOD, Department of Anesthesia, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India

Corresponding Author:
Dr. Zareen Fatima
Post Graduate Junior Resident 3 rd year, Department of Anesthesia, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India

A comparative study between nalbuphine with Bupivacaine versus bupivacaine alone in USG guided axillary Brachial plexus block

Dr. Zareen Fatima, Dr. Ruchira Sarkar, Dr. Neeraj and Dr. Vishal Arora

DOI: https://doi.org/10.33545/26643766.2023.v6.i3b.417

Abstract
Background: Nalbuphine, a potent analgesic with both kappa agonist and antagonist properties, is a derivative of 14-hydroxymorphine. Extensive research has been conducted on the use of nalbuphine as an adjuvant to local anesthetics, specifically in axillary brachial plexus blocks, both in intravenous and spinal applications. The study aimed to assess effectiveness of nalbuphine in axillary brachial plexus blocks when used in conjunction with local anaesthetics.
Patients and Method: In two groups of 28 patients each, under axillary and branchial plexus block, 62 cases preplanned for elective forearm and hand surgery were assigned at random. The first group received 25 ml (0.5%) of bupavacaine combined with 1 ml of normal saline (NS), whereas the other received 25 ml (0.5%) bupivacaine along with 1 ml (20mg) nalbuphine. The study examined the initiation time and duration of both sensory and motor block, and the effectiveness of analgesia following the surgery.
Results: The nalbuphine group demonstrated a significant increase in motor block length (402.59±18.56) when compared to placebo group (348.70 ± 28.019), with a p-value of less than 0.001. Similarly, the nalbuphine group experienced a significantly longer sensory duration (709.14±21.04) compared to placebo group (605.18±25.33), also with a p-value of less than 0.001. The administration of nalbuphine did not affect the onset time of the blockade. Additionally, the nalbuphine group exhibited a statistically significant prolongation of the analgesic effect (825.18±32.45) when comparison done to the placebo group (718.14±44.57), with a p-value > 0.01.
Conclusion: According to the current study, axillary brachial plexus block patients who receive 20 mg of nalbuphine in addition with bupivacaine experience a considerable extension of their analgesic time. The length of both sensory and motor blocks is also greatly increased.

Keywords: Bupavacaine combined, plexus block, analgesic

1. Introduction
Background
A practical and dependable regional anesthetic treatment with many uses is the brachial plexus block. For some patients, it is a good substitute for general anesthesia today. The brachial plexus block is one of the mostly used nerve blocks for the upper extremity. It offers several advantages over general anesthesia, such as minimizing the potential side effects associated with anesthetic medications and reducing the stress caused by laryngoscopy and tracheal intubation. Furthermore, patients undergoing a brachial plexus block can experience a more comfortable postoperative period, as it helps alleviate issues like upset stomach, central nervous system depression, and acute surgical pain [1].
Compared to other brachial plexus block techniques, the axillary brachial plexus block offers a number of benefits. It offers comprehensive and dependable anesthesia for surgeries on the upper limbs. It is carried out at the division level, where plexus is most compactly displayed. [2]. The local anesthetist's objective was to improve the effectiveness of local anesthetics by extending block duration and reducing the hazards of toxicity of local anesthetics. Various adjuvants, such as opioids, dexamethasone, and clonidine, are added local anesthetics to achieve these goals and prolong the block duration while minimizing toxicity [3, 4].
Numerous studies investigated the effects of nalbuphine added as an adjunct to local anesthetics in spinal, epidural, and local intravenous blocks. The consistent findings from these studies demonstrate that nalbuphine is an effective adjuvant, as it substantially

lengthens the duration of the block.

Nalbuphine, a potent analgesic with a unique pharmacological profile, is derived from 14-hydroxymorphine. It acts as a dual mu (μ) antagonist and kappa (k) agonist. Although both morphine and nalbuphine exhibit similar analgesic effects, nalbuphine has a greater impact on reducing respiratory depression. This means that nalbuphine can provide and maintain analgesic benefits similar to μ opioid-based drugs while reducing the associated negative effects, such as respiratory depression [6].

2. Objective of Study

Nalbuphine has been investigated as a potential adjunct to local anesthetics in spinal, epidural, and local intravenous regional blocks. This research investigated the impacts of combining nalbuphine in combination bupivacaine against the use of bupivacaine alone. The objective was to determine the efficacy of nalbuphine as a supplementary agent to local anesthetics, specifically in axillary brachial plexus blocks for elective upper limb procedures. The primary focus of the present research assesses the utility of nalbuphine as an adjunct in peripheral nerve blocks.

3. Patients and Methods

From June 2021 to December 2022, a double blinded, randomized, controlled clinical trial took place at Integral University. The research involved 62 cases, both males and females, with ASA physical status I and II, aged ranged from 18 to 60 years. These patients were planned to undergo elective forearm and hand surgery in the operating rooms of the orthopedic and plastic surgery departments. Approval for the study was obtained from the departmental scientific and ethical council before patient enrollment.

Patients who refused the procedure, had a history of bleeding, were taking oral anticoagulants, had neurological issues affecting the branchial plexus, were allergic to local anaesthetics, had local infection at injection site, were taking any sedatives or antipsychotic, and had a body mass index higher than thirty-five were all at risk for complications.

Two equal study groups were randomly assigned to the patients. The senior anesthesia personnel maintained the opaque sealed envelopes containing the randomization sequence. Written informed consent was provided by the patients. Following the receipt of patients' consent, the envelopes containing the treatment assignments were unsealed. Two groups of patients will be formed.

Group C: Thirty-one participants in the control group will be given 25 ml of 0.5% bupivacaine and 1 ml of NS.

Group N: Thirty-one participants will receive 1 ml (20mg) of nalbuphine and 25 ml of 0.5% bupivacaine in the nalbuphine group.

a. Primary Outcomes

1. The initiation of sensory and motor blockade.
2. The duration sensory and motor blockade.
3. The duration of analgesia (time until the first request for analgesic medication).

b. Secondary Outcome Parameters

1. Blood Pressure (BP).
2. Respiratory rate.
3. Oxygen saturation (SpO_2).

Every patient underwent a thorough preoperative evaluation that included obtaining their medical history, getting a physical, and going over the findings of regular tests. The visual analogue pain score (VAS), which ranges from zero to ten (intolerable pain), was explained to all candidates.

A 20 gauge IV cannula was placed into a peripheral vein in the contralateral arm upon entry to the preparation area. Patients were put to sleep with 0.01 to 0.05 mg/kg of intravenous midazolam, and when needed, 1 mcg /kg of intravenous fen-tanyl was given (to maintain moderate sedation; awakenable on demand). Participants were then accompanied to the operating room, where they underwent the application of essential monitoring equipment, including an electrocardiogram (ECG), a non-invasive blood pressure monitor (NIBP), and a pulse oximeter (SpO2). Baseline measurements of heart rate, blood pressure, oxygen saturation, and respiration rate were documented prior to administering the block.

The patient assumed a supine position, with their head inclined at a 45-degree angle in the opposite direction. An ultrasonic machine, the Mindray M7, equipped with a 12 MHz linear probe, was employed for the procedure. Prior to commencement, the skin was prepped and a local anesthetic was administered for numbing. Utilizing ultrasound technology, the subclavian artery, first rib, pleura, and brachial plexus cluster were identified. Subsequently, a 22-gauge, 5 cm echogenic B. Braun needle was inserted under ultrasound guidance, following a medial-to-lateral trajectory.

Throughout the procedure, BP and heart rate will be observed for the time period of 15 min for the initial 15 minutes, and subsequently after 5 mins. Beyond 30 minutes after the infusion of local anesthetics, inadequate sensory and motor blockade will be regarded as an ineffective block.

After the completion of the procedure, within the first two hours following surgery, we assessed and recorded the initiation of sensory and motor blockade, as well as the length of both motor and sensory blockade. The duration of analgesia was determined by interviewing the patient and noting the time of their first request for analgesic medication. Any negative effects were noted and patients were carefully evaluated. If patients reported postoperative pain with a Visual Analog Scale (VAS) score exceeding 3, rescue analgesia was provided. Until the VAS score decreased below 3, rescue analgesia consisted of pethidine (1 mg/kg), paracetamol (1 gm IV drip), and/or diclofenac sodium (75 mg IM).

Statistical Analysis

A total of 62 participants will be included in the study to detect a minimally clinical significant rise of 10% in the length of sensory blockade. The participants will be categorized into two groups, with 31 participants in every group. The calculations consider various assumptions, including an average time span of sensory block with bupivacaine of 4 hrs. The study will employ two-tailed α and β error probabilities of 0.05 and 0.2 (power of 80%), respectively.

The SPSS programme was used to conduct the statistical analysis. The numbers and percentages, as well as averages and standard derivations, were used to present the data. The t-test was used to assess the difference between the means. Statistical significance defined as a P value less than 0.05.

3. Results

Overall, 72 people were evaluated for the study. Ten patients were excluded, six of them failed to meet the inclusion criteria and four participants declining to participate. Finally, 62 patients with ASA physical status I and II were included in the research; and of both sexes and ranged in age from 18 to 60. These patients met the inclusion criteria and were undergoing forearm and hand surgery in the orthopedic and plastic surgery operating rooms of Integral Hospital. It is important to note that every patient who registered for the research successfully completed it. From among those patients, two groups of 31 patients each were chosen at random.

No statistically significant differences were found between the two study groups regarding demographic variables, including age, gender, weight, ASA classification, and duration of the operation. It is noteworthy that approximately 75% of the study participants belonged to ASA class I. Table1.

The results pertaining to the initiation of sensory and motor blocks indicated that the nalbuphine group exhibited a relatively quick onset for both motor and sensory blocks. However, there was no statistical significant difference was seen, as shown in Table2.

The study revealed a statistically significant difference in the duration of motor block between the nalbuphine group and the control group. The motor block was found to be significantly longer in the nalbuphine group compared to the control group, with a p-value of 0.001. Table 3.

When the comparison was done between nalbuphine and placebo group, statistically significant differences (p-value 0.001) were found, indicating a delayed regression of sensory block.

A substantial difference between the nalbuphine group and the placebo group was discovered when comparing the length of analgesia after the administration of a nerve block (p-value 0.001). Table4.

All of the patients in the tested groups responded favorably to the nerve blockade that was delivered. In the Post-Anesthesia Care Unit (PACU), none of the participants needed rescue analgesics during or after surgery. Both block-related hemodynamic changes and local anesthetic toxicity were absent.

Table 1: Demographic data.

	Nalbuphin group (n=31)	**Control group (n=31)**
Age(years)	48±6.5	50±5.4
Sex		
1Male	17 (57%)	18 (64%)
Female ASA† classification	14 (43%)	13 (36%)
I	21(71.5%)	23(78.5%)
II	10(28.5%)	8(21.5%)
Weight (Kg)	68±1.12	66±0.96
Duration of surgery (hours)	2.3±1.15	2.5±1.26

The data was represented as mean ± SD or no. of cases (%). The "ASA" stands for the American Society of Anaesthesiologists.

Table 2: Onset of sensory and motor blockade.

	Group-N (n=31)	**Group-C (n=31)**	**p-value**
Onset of sensory block (min.)	9.56±0.78	10.18±1.33	0.063
Onset of motor block (min.)	15.6±1.09	17±1.40	0.126

*p value<0.05isconsideredstatisticallysignificant

Table 3: Duration of sensory and motor blockade.

	Group-N(n=28)	**Group C(n=28)**	***p*-value**
Duration of sensory block(min.)	718.14±44.57	605.18±25.33	<0.001
Duration of motor block(min.)	402.59±18.56	348.70±28.019	<0.001

*p value<0.05isconsideredstatisticallysignificant.

Table 4: Analgesia duration.

	Group N(n=28)	**Group C(n=28)**	***p*-value**
Duration of analgesia (min.)	825.18±32.45	718.14±44.57	<0.001

**p* value<0.05 is considered statistically significant.

4. Discussion

The current research investigations reported that motor block was considerably prolonged (402.59±8.56) when 20 mg of nabulphine was administered with 0.5% bupivacaine for supra clacivular branchial plexus block as compared to placebo group (348.70±28.019). The nalbuphine group exhibits a notable extension in the time span of sensory block (718.14±44.57) compared to placebo group (605.18±25.33). Additionally, the nalbuphine group demonstrates a significantly longer duration of the analgesic effect (825.18±32.45) compared to the placebo group (718.14±44.57).

In previous studies, nalbuphine was tested as a local anaesthetic adjuvant in epidural, caudal, and intrathecal anesthesia [7, 8]. After performing a thorough assessment of the literature, we found that there aren't many published studies that specifically examine nalbuphine's effects when used in conjunction with local anaesthetics to treat peripheral nerve blocks.

Nalbuphine, in comparison to morphine, exhibits a moderate analgesic effect due to its mixed kappa-agonist and mu-antagonist opioid structure. This unique structure enables

nalbuphine to bind to kappa-opioid receptors, resulting in sedation, analgesia, cardiovascular stability, and minimal respiratory depression. Notably, butorphanol and nalbuphine have several chemical properties, including their mode of action oponiods receptors and the inhibition of neuronal serotonin synthesis [9]. When opiate receptors are activated, adenylyl cyclase was inhibited; potassium channels opened, and closes calcium channels. This causes the cell membrane to become hyperpolarized and prevents the transmission of pain signals [10].

For improving the quality length of anesthesia and post-operative analgesia, it has been usual practise to mix opoids such as fentanyl, morphine, tramadol, and butorphanol with local anaesthetics in peripheral. Ranjit *et al*., reported that when combination with bupivacaine, butorphanol prolonged the duration of supraclavicular brachial plexus block cases elective hand and forearm surgery. The researchers also provided an explanation for how butorphanol impacts central nervous system neurons through the stimulation of opioid receptors [10]. Kapral *et al*., performed the utilization of mepivacaine and tramadol in blocking the axillary branchial plexus resulted in a significant prolongation of the block without any observed adverse effects. The combination of 100 mg of tramadol and 1% mepivacaine was found to be effective. The researchers also provided an explanation for how tramadol and its metabolites impact opiate receptors [11]. Wajima *et al*. study found that continuous local infusion butaphanol into branchial plexus sheath was more successful at relieving pain than continuous intravenous systemic administration [12]. Wajima *et al*., it was discovered that 2 mg of butorphenol combined with 0.5% mepivacaine produced satisfactory postoperative analgesia following upper limb surgery [13]. Previous studies have collectively shown that various opioids have beneficial effects on peripheral nerves by activating opioid receptors.

Our findings align with those of Veena Chatrath *et al*., who conducted a study investigating the postoperative analgesic effects of epidurally administered tramadol and nalbuphine in cases undergoing lower limb orthopedic surgeries. Their study revealed that the nalbuphine group exhibited superior surgical analgesia, a lower incidence of adverse effects, and fewer complications compared to the tramadol group [14]. Yoon *et al*., 60 cases undergoing caesarean sections received either 1 mg of morphine, 1 mg of nalbuphine, or a combination of 0.1 mg of morphine and 1 mg of nalbuphine along with 10 mg of bupivacaine. The morphine group and morphine with nalbuphine group demonstrated prolonged duration of effective analgesia compared to the nalbuphine-alone group [15]. Hala *et al*. conducted a research involving 60 female patients undergoing elective cesarean deliveries under spinal anesthesia, the effects of intrathecal nalbuphine and fentanyl were compared. The study concluded that neither intrathecal nalbuphine (0.8 mg) nor intrathecal fentanyl (25 µg) significantly differed in terms of prolonging early post-operative analgesia [16]. In a study conducted by Shela Shakkoh *et al*., preservative-free nalbuphine (0.8 mg) was used as an adjuvant to intrathecal hyperbaric bupivacaine (0.5%) in lower abdomen and lower limb surgeries. The postoperative analgesic effect of this combination was compared to the use of hyperbaric bupivacaine (0.5%) alone under spinal anesthesia. The study concluded that the addition of nalbuphine as an adjuvant in spinal anesthesia provided effective postoperative analgesia, optimal intraoperative sedation, and did not result in significant side effects [17]. Culebras *et al*. carried out a research involving 90 obstetric cases undergoing caesarean sections, different intrathecal doses of nalbuphine (0.2 mg, 0.8 mg, and 1.6 mg) were evaluated. The research demonstrated that 0.8 mg dose of nalbuphine was the most effective [18]. Arghya Mukherjee *et al*., in his investigations found that that administering 0.4 mg of nalbuphine as an adjuvant to 0.5% hyperbaric bupivacaine in spinal anesthesia significantly prolonged early postoperative analgesia without increasing the risk of side effects. The researchers suggested the administration of 0.4 mg of nalbuphine intravenously in combination with 12.5 mg of 0.5% hyperbaric bupivacaine for spinal anesthesia in patients undergoing lower limb orthopedic surgery [19]. Maha M.I. *et al*., reported that the effects of nalbuphine and tramadol were similar as adjuvants to lidocaine in intravenous regional anesthesia. However, nalbuphine demonstrated superior performance in extending the duration of postoperative analgesia compared to tramadol [20].

5. Conclusion

According to the current study, adding 20 mg of nalbuphine to bupivacaine during an axillary branchial plexus block for procedures on the forearm and hand greatly lengthens the duration of post-operative analgesia as well as the duration of sensory and motor blocks.

6. Conflict of Interest

No Conflict of Interest.

7. References

1. Singh A, Gupta R, Vashisth M, Singh S, Kumari A, Aujla KS. Comparison of Effectiveness of Brachial Plexus Block by Supraclavicular and Axillary Approach Alone or in Combination. Journal of Anesthesiology Clinical Pharmacology. 2010;26:31-34.
2. Neal JM, Gerancher JC, Hebl JR, Ilfeld BM. Upper Extremity Regional Anesthesia. Regional Anesthesia and Pain Medicine. 2009;34:134-170. http://dx.doi.org/10.1097/AAP.0b013e31819624eb
3. Kim YJ, Lee GY, Kim DY, Kim CH, Baik HJ, Heo S. Dexamathasone Added to Levobupiva-caine Improves Postoperative Analgesia in Ultrasound Guided Interscalene Brachial Plexus Blockade for Arthroscopic Shoulder Surgery. Korean Journal of Anesthesiology. 2012;62:130-134. http://dx.doi.org/10.4097/kjae.2012.62.2.130
4. Khasar SG, Green PG, Chou B, Levine JD. Peripheral Nociceptive Effects of Alpha 2-Adrenergic Receptor Agonists in the Rat. Neuroscience. 1995;66:427-432. http://dx.doi.org/10.1016/0306-4522(94)00562-J
5. Gunion MW, Marchionne AM, Anderson TM. Use of the Mixed Agonist-Antagonist Nalbuphine in Opiod Based Analgesia. Acute Pain, (2004) 6, 29-39. http://dx.doi.org/10.1016/j.acpain.2004.02.002
6. Jyothi B, Gowda S, Shaikh SI. A Comparison of Analgesic Effect of Different Doses of Intrathecal Nalbuphine Hydrochloride with Bupivacaine and Bupivacaine Alone for Lower Abdominal and Orthopedic Surgeries. Indian Journal of Pain. 2014;28:18-23. http://dx.doi.org/10.4103/0970-5333.128881
7. Saryazdi H, Yazdani A, Sajedi P, Aghadavoudi O.

Comparative Evaluation of Adding Different Opiates (Morphine, Meperidine, Buprenorphine, or Fentanyl) to Lidocaine in Duration and Quality of Axillary Brachial Plexus Block. Advanced Biomedical Research. 2015;4:232-237.
8. Wajima Z, Nakajima C, Kim C. Compared with Brachial Plexus Infusion of Butorphanol for Postoperative Analgesia. British Journal of Anaesthesia. 1995;74:392-395. http://dx.doi.org/10.1093/bja/74.4.392
9. Yeh YC, Lin TF, Lin FS, Wang YP, Lin CJ, Sun,W.-Z. Combination of Opioid Agonist and Agonist-Antagonist: Patient Controlled Analgesia Requirement and Adverse Events among Different-Ratio Morphine and Nalbuphine Admixtures for Postoperative Pain. British Journal of Anesthesia. 2008;101:542-548. http://dx.doi.org/10.1093/bja/aen213
10. Gear RW, Miaskowski C, Gorden NC. The Kappa Opioid Nalbuphine Produces Gender and Dose De-pendent Analgesia and Antianalgesia in Patients with Postoperative Pain. Pain, 1999;83:339-345. http://dx.doi.org/10.1016/S0304-3959(99)00119-0
11. Acharya R, Jena M, Mishra S, Rath SK. Effect of Butorphanol versus Placeboas Adjuvant to Bupiva-caine for Supraclavicular Brachial Plexus Blockade. International Journal of Applied Pharmaceutics, 2014;6:8-10.
12. Kapral S, Gollmann G, Waltl B, Likar R, Sladen RN, Weinstabl C. Tramadol Addedto Mepivacaine Prolongsthe Duration of an Axillary Brachial Plexus Blockade. Anesthesia & Analgesia. 1999;88:853-856.
13. Wajima Z, Shitara T, Nakajima Y. Continuous Brachial Plexus Infusion of Butorphanol-Mepivacaine Mixtures for Analgesia after Upper Extremity Surgery. British Journal of Anaesthesia, 1997;78:83-85. http://dx.doi.org/10.1093/bja/78.1.83
14. Chatrath V, Attri JP, Bala A, Khetarpal R, Ahuja D, Kaur S. Epidural Nalbuphine for Postoperative Analgesiain Orthopedic Surgery. Anesthesia: Essays and Researches. 2015;9:326-330. http://dx.doi.org/10.4103/0259-1162.158004
15. Gomaa HM, Mohamed NN, Zoheir HAH, Ali MS. A Comparison between Post-Operative Analgesia after Intrathecal Nalbuphine with Bupivacaine and Intrathecal Fentanyl with Bupivacaine after Cesarean Section. European Journal of anesthesiology. 2014;30:405-410.
16. Yoon JY, Jee YS, Hong JY. A Comparison of Analgesic Effects and Side Effects of Intrathecal Morphine, Nalbuphine and Morphine-Nalbuphine Mixture for Pain Relief during a Caesarean Section. Korean Journal of Anesthesiology. 2002;42:627-633. http://dx.doi.org/10.4097/kjae.2002.42.5.627
17. Shakooh S, Bhosle P. Intrathecal Nalbuphine: An Effective Adjuvant for Post Operative Analgesia. Inno-vative Journal of Medical and Health Science. 2014;4:79-82.
18. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N. Intrathecal Nalbuphine as an Adjuvant to Subarachnoid Block: What Is the Most Effective Dose. Anesthesia: Essays and Researches. 2012;5:171-175.
19. Culebras X, Gaggero G, Zatloukal J, Kern C, Marti, RA. Advantages of Intrathecal Nalbuphine, Compared with Intrathecal Morphine, after Cesarean Delivery: An Evaluation of Postoperative Analgesia and Adverse Effects. Anesthesia & Analgesia. 2000;91:601-605. http://dx.doi.org/10.1213/00000539-200009000-00019
20. Youssef MMI, ElZayyat NS. Lidocaine-Nalbuphine versus Lidocaine-Tramadol for Intravenous Regional Anesthesia. Ain-Shams Journal of Anesthesiology, 2014;7:198-204. http://dx.doi.org/10.4103/1687-7934.133441

How to Cite This Article
Z Fatima, R Sarkar, Neeraj, J Singh. A comparative study between nalbuphine with Bupivacaine versus bupivacaine alone in USG guided axillary Brachial plexus block. International Journal of Medical Anesthesiology. 2023;6(3):95-99