Evaluating The Utilization Of Nalbuphine As An Adjuvant To 0.5% Bupivacaine For Ultrasound-Guided Supraclavicular Brachial Plexus Blockade: A Study In A Tertiary Care Hospital, Dhaka, Bangladesh

Mir Masud Royhan^{*1}, Nazmul Ahsan Siddiqi Rubel², Abul Ishrat³, Md. Anisur Rahman⁴, Nazem Ahmed⁵

¹MBBS, Diploma in Anesthesiology, Junior Consultant (Anaesthesiology), Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka.

²MBBS, Diploma in Anaesthesiology, FCPS (Anaesthesiology), Junior Consultant, Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka

³MBBS, MD (Anaesthesiology), Assistant Surgeon, Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka.

⁴MBBS, Diploma in Anaesthesiology, Junior Consultant (Anaesthesiology), UHC, Agoilzhara, Barishal ⁵MBBS, Diploma in Anaesthesiology, Junior Consultant, Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka.

Abstracts

Introduction: Supraclavicular block (SCB) has demonstrated remarkable post-operative patient outcomes in upper limb surgeries. Bupivacaine, a long-acting regional anesthetic, exhibits efficacy that can be influenced by the concomitant administration of additives.

Objective: The primary objective of this study was to evaluate the effectiveness of supraclavicular block using 0.5% bupivacaine compared to the adjunctive administration of additives, as well as to assess any associated complications.

Methods and Materials: This prospective study enrolled 62 patients aged 18-60 years with physical status I to II of both gender, aged 18–58 years with body mass index (BMI) <25 kg/m2. Patients underwent elective forearm and hand surgeries, with written consent and ethical approval. Randomized into two groups, ultrasound-guided supraclavicular brachial plexus block was performed using bupivacaine alone (Group 1) or with nalbuphine (Group 2). Sensory and motor blocks, analgesia duration, patient satisfaction, and adverse effects were evaluated. The study followed ethical guidelines and performed statistical analyses for data evaluation.

Results: The study included 62 participants undergoing forearm and hand surgeries, evaluating nalbuphine as an adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block. The majority were aged 15-30 years (41.94%), with 56.45% males and 43.55% females. The population consisted of business professionals (25.81%), farmers (24.19%), service holders (29.03%), and housewives (20.96%). Smokers accounted for 53.23%, and 54.84% resided in urban areas. Group 2 (n=31) had longer durations of motor block and analgesia compared to Group 1 (n=31). Patient satisfaction was high (91.93%), with a willingness to recommend the procedure. Dissatisfaction reasons included pain or discomfort during the block (83.33%) and transient paraesthesia (16.67%).

Conclusion: Nalbuphine (10 mg) added to 0.5% bupivacaine for supraclavicular brachial plexus block in forearm and hand surgeries extends analgesia duration without adverse effects. Ultrasound guidance ensures complication-free procedures, highlighting nalbuphine as a potential adjuvant option for local anesthetics.

Keywords: Brachial plexus block, Nalbuphine, supraclavicular approach, ultrasound guidance, Bupivacaine

Date of Submission: 08-09-2023

Date of Acceptance: 18-10-2023

I. INTRODUCTION

Supraclavicular brachial plexus blockade is an effective and reliable alternative to general anaesthesia for upper limb surgeries with minimal side effects^{1, 2}. The brachial plexus is formed by the ventral rami of C5-T1, occasionally with small contributions by C4 and T2³. Ultrasound provides a more precise block and decreases tissue injury. It also decreases the drug volume and systemic toxicity related to the drug. It helps for better visualization and localization of the brachial plexus⁴⁻⁵. Bupivacaine is a local anesthetic that relieves pain by blocking the transmission of pain signals to the dorsal horn. However, it also has a definite risk of systemic

toxicity, especially when used for brachial plexus block. To reduce the dose and incidence of adverse reactions, various adjuvants are used to augment the analgesic efficacy of bupivacaine⁶. Brachial plexus block is associated with excellent patient outcomes postoperatively for upper limb surgery, these benefits being; superior postoperative analgesia and recovery compared with that of general anaesthesia and opioid analgesia, and providing similar quality of postoperative analgesia comparable to epidural analgesia⁷. 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. Opioids were affected either by action on opioid receptors or finally by their systemic absorption. Nalbuphine, an opioid agonist–antagonist, is used as an adjuvant to local anesthetic for various regional anesthetic techniques due to its affinity to κ –opioid receptors to enhance the duration of analgesia. It is widely studied as an adjuvant to local anesthetics in central neuraxial techniques by epidural, caudal, and intrathecal routes⁸. Nevertheless, despite extensive literature research, there appears to be a scarcity of published data investigating the impact of nalbuphine when used as an adjuvant to local anesthetics in peripheral nerve blocks. In light of this, the objective of this study was to evaluate the clinical effectiveness and safety of nalbuphine as an adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block, utilizing ultrasound guidance, in a diverse range of forearm and hand surgical procedures.

II. OBJECTIVES

The main objective of this study was to evaluate the effectiveness of supraclavicular block using 0.5% bupivacaine alone in comparison to the addition of adjunctive additives. Furthermore, the study aimed to assess any potential complications associated with the procedure and additives. By conducting this research, a comprehensive evaluation of the efficacy and safety of the supraclavicular block with or without additives could be achieved.

III. METHODS AND MATERIALS

Study design: This prospective observational study was undertaken to evaluate the utilization of nalbuphine as an adjuvant to 0.5% bupivacaine for ultrasound-guided supraclavicular brachial plexus blockade.

Study period: This study was conducted during the period from 01 April 2022 to 30 September 2022 (06 months).

Place of study: The study was carried out at Sheikh Hasina National Institute of Burn and Plastic Surgery (SHNIBPS), Dhaka.

Study population: This prospective study enrolled 62 patients with a physical status I to II of both gender, aged between 18 and 60 years with body mass index (BMI) <25 kg/m2. The patients were scheduled for elective forearm and hand surgeries in orthopedic and plastic surgical operation theaters. Prior to participation, written informed consent was obtained from each patient, following approval from the Institutional Ethics Committee. Patients with clinically significant coagulopathy, infection at the injection site, known allergy to local anesthetics, preexisting neuromuscular, severe cardiovascular or pulmonary disease, renal or hepatic disorders, refusal to undergo the technique, or inability to visualize the brachial plexus with ultrasound guidance were excluded from the study.

Patients who were taking psychotropic medications or receiving chronic analgesic therapy, other than simple analgesics, were also excluded. The patients were randomized into two equal groups of 32 patients each, using a computer-generated random number table. Group 1 received 20 mL of 0.5% bupivacaine with 1 mL of normal saline, while Group 2 received 20 mL of 0.5% bupivacaine with 1 mL of nalbuphine (10 mg). The study drug solutions were prepared by a resident anesthetist who was not involved in data collection, maintaining the blinding of the study.

The ultrasound-guided supraclavicular brachial plexus block was performed using a transportable ultrasound system and a high-frequency linear transducer. The study drug solution was administered around the brachial plexus under ultrasound imaging guidance, ensuring negative aspiration to avoid accidental intravascular injection. The onset time of sensory and motor blocks, duration of motor block, and duration of analgesia were assessed and compared between the two groups.

All patients underwent continuous monitoring of vital parameters, including blood pressure, heart rate, electrocardiogram (ECG), and pulse oximetry, throughout the perioperative period. Patient satisfaction was assessed, and any reasons for dissatisfaction or non-recommendation were documented. Any adverse effects or complications were managed in accordance with the established clinical protocol. Postoperative pain levels were measured using the visual analog scale (VAS), and tramadol and ondansetron were administered as rescue analgesia when necessary. The study adhered to a rigorous methodology, following ethical guidelines and ensuring participant and investigator blinding. Statistical analyses were performed to assess the data and determine the significance of the findings.

Statistical Analysis: The sample size for this study was calculated using standard computer programs, which determined that 31 patients should be included in each group. This calculation aimed to detect a clinically

significant difference of more than 20% in the duration of block and postoperative analgesia between the groups, with an alpha error of 0.05, 80% power, and 95% confidence level. Accounting for a potential dropout rate of 5%, the final sample size was determined to be 60 patients to ensure robust validation of the results. The collected data were presented as mean and standard deviation, with the latter, considered the most reliable predictor. Statistical analysis was conducted using SPSS 20.0 software. Various statistical tests, including Student's t-test, Chi-square test, and Mann-Whitney U-test, were employed to compare the observed data between the groups. A significance level of P < 0.05 was used to determine statistical significance.

Age distribution	Population	Percentage (%)
15-30	26	41.94
31-45	19	30.65
46-60	17	27.41
Gender		
Male	35	56.45
Female	27	43.55
Profession		
Business	16	25.81
Service holder	18	29.03
Farmer	15	24.19
Housewife	13	20.96
Smoke		
Smoker	33	53.23
Non-Smoker	29	46.77
Area		
Rural	28	45.16
Urban	34	54.84

IV. RESULTS Table 1: Demographic Profile of Study Population (n=62):

Table-1 displays the demographic profile of the study population consisting of 62 individuals, which is relevant to the investigation of "Nalbuphine as an Adjuvant to 0.5% Bupivacaine for Ultrasound-guided Supraclavicular Brachial Plexus Blockade." The population encompasses various age groups, with the majority falling within the 15-30 age range (41.94%). Males comprise 56.45% of the population, while females make up 43.55%. Professionally, the population includes business professionals (25.81%), farmers (24.19%), service holders (29.03%), and housewives (20.96%). Smokers account for 53.23% of the population, with non-smokers representing 46.77%. In terms of area, 45.16% reside in rural areas, while 54.84% live in urban settings.

Table 2:	Group-wise	patients	profile	(n=62)
----------	-------------------	----------	---------	--------

Data/group	Group-1	Group-2
Male	19	16
Female	12	15
Weight (kg)	57.8±9.7	63.7±7.8
BMI (kg/m ²)	19.10±2.78	20.61±3.21
ASA grade (I/II)	21/9	23/7
Duration of surgery (min)	168.17±16	165.35±20

Table-2 present the study population consisting of 62 patients, focusing on their demographic profile and surgical characteristics. The table reveals that Group-1 consisted of 19 males and 12 females, while Group-2 included 16 males and 15 females. When examining weight, Group-1 exhibited a mean weight of 57.8 kg with a standard deviation of 9.7, whereas Group-2 had a slightly higher mean weight of 63.7 kg with a standard deviation of 7.8. The body mass index (BMI) measurements showed that Group-1 had an average BMI of 19.10 kg/m² with a standard deviation of 2.78, while Group-2 had an average BMI of 20.61kg/m² with a standard deviation of 3.21. Assessing the ASA grade, Group-1 had 23 patients classified as ASA grade I and 9 patients as ASA grade II, while Group-2 had 25 patients classified as ASA grade I and 7 patients as ASA grade II. Lastly, the table provided the duration of surgery, indicating that Group-1 had a mean duration of 168.17 minutes with a standard deviation of 16, while Group-2 had a mean duration of 165.35 minutes with a standard deviation of 20.

Parameter/groups	Group 1	Group 2	P-Value
Onset time of sensory block (min)	10.36±1.7	9.57±1.5	0.76
Onset of motor block (min)	18.16±1.30	$14.10{\pm}1.24$	0.49
Duration of motor block (min)	257.69±30.19	278.53±34.61	0.038*
Duration of analgesia (min)	341.31±21.42	481.53±42.45	0.001**

Table 3. Sensor	y and motor blockade characteristics of brachial plexus block
Table 5. Sensor	and motor blockade characteristics of brachial plexus block

Table-3 presents the sensory and motor blockade characteristics of the brachial plexus block in Group 1 and Group 2. The onset time of sensory block was similar between the groups, with Group 1 having an average onset time of 10.36 minutes and Group 2 with 9.57 minutes. The onset of motor block was slightly faster in Group 2 (14.10 minutes) compared to Group 1 (18.16 minutes). The duration of motor block was significantly longer in Group 2 (278.53 minutes) compared to Group 1 (257.69 minutes). Moreover, the duration of analgesia was significantly higher in Group 2 (481.53 minutes) compared to Group 1 (341.31 minutes).

 Table 4. Patient satisfaction (n=62)

	Number of patients	Percentage (%)
Patient satisfaction		
Satisfied	57	91.93
Unsatisfied	5	8.07
Will undergo surgery with same procedure/recommend it to others?		
Yes	57	91.93
No	5	8.07
Reason for unsatisfaction/non-recommendation		
Pain/discomfort during block procedure	5	83.33
Paraesthesia lasting for 24 hrs	1	16.67

Table-4 provides information on patient satisfaction regarding the brachial plexus block procedure. Out of the total study population of 62 patients, 91.93% (57 patients) reported being satisfied with the procedure, while 8.07% (5 patients) expressed dissatisfaction. Similarly, 91.93% (57 patients) stated that they would undergo the same procedure again or recommend it to others, while 8.07% (5 patients) indicated otherwise. Among the reasons for dissatisfaction or non-recommendation, 83.33% (5 patients) mentioned pain or discomfort during the block procedure, and 16.67% (1 patient) reported experiencing paraesthesia lasting for 24 hours.

V. DISCUSSION

A nalbuphine dose of 20 mg was chosen as per the recommendation in the textbook as well as previous research¹⁰. Sáinz López et al. demonstrated that ultrasound guidance enabled the use of reduced doses of local anesthetic for supraclavicular brachial plexus block to minimize the risks of the systemic toxicity of local anesthetic drugs¹¹. In the present study, we used only 100 mg of bupivacaine to establish the effective block and our assessment was in accordance with their findings. Different opioid medications have been added to local anaesthetic to improve the quality and duration of postoperative analgesia of peripheral nerve blocks¹². Numerous prior studies have endeavored to investigate the potential enhancement of clinical efficacy in peripheral nerve blocks by incorporating opioids alongside local anesthetics. These studies have shown that various opioids effectively interact with peripheral nerves by stimulating opioid receptors. However, their usage has been accompanied by undesirable side effects. Tramadol and fentanyl have frequently been employed as adjuvants to local anesthetic drugs in brachial plexus blocks¹³. A systemic review of various adjuvants for brachial plexus block suggested that nalbuphine appeared to possess greater analgesic efficacy with minimal adverse effects. Nalbuphine is a mixed agonist and μ -antagonist opioid, and its affinity to kopioid receptors results in analgesia, sedation, and cardiovascular stability with minimal respiratory depression. It may potentiate local anesthetic action through central opioid receptor-mediated analgesia by peripheral uptake of nalbuphine to the systemic circulation. Young et al. demonstrated that opioid receptors and various macromolecules in the nerve undergo axonal flow¹⁴. Opioids penetrate the nerve membrane and act at the dorsal horn. Laudren showed that proteins undergo bidirectional axonal transport and speculated that these receptors circulate endorphins, their endogenous ligands, in addition to exogenous opioids which proves that opioids act directly on peripheral nervous system¹⁵. The findings of the current study demonstrated that the addition of nalbuphine (10 mg) to 20 mL of 0.5% bupivacaine significantly improved the quality of supraclavicular brachial plexus block and prolonged the duration of both sensory and motor block. The study concluded that butorphanol prolonged the duration of brachial plexus block¹⁶. In the present study, there was also a significant increase in the duration of analgesia in patients who received nalbuphine as an adjuvant (481.53 ± 42.45 min) as compared to another group (341.31 ± 21.42 min). This enhancement may be due to the synergistic action of nalbuphine with bupivacaine. Viel et al. showed that injection buprenorphine into the brachial plexus sheath using supraclavicular technique is an efficient way to

control postoperative pain after upper limb surgery¹⁷. Youssef and E 1 Zayyat 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 postoperative analgesia¹⁸. Abdelhaq and Elramely¹⁹ 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 the both sensory and motor block along with prolonged postoperative analgesia. The present study is supported by Chiruvella S et al., who explained sedation by nalbuphine on the basis of some amount of systemic absorption of drugs²⁰. In our current study, we observed a statistically significant prolongation in the duration of sensory and motor block, as well as the duration of analgesia, even with reduced doses of 10 mg nalbuphine combined with 20 ml of 0.5% bupivacaine for upper arm surgeries. The advantages offered by nalbuphine were not accompanied by any hemodynamic variations or adverse events. Since nalbuphine acts as an agonist to κ receptors and an antagonist to μ receptors, it lacks side effects such as pruritus, nausea, vomiting, and respiratory depression. Throughout the study, there were insignificant differences in intraoperative changes in vital parameters and oxygen saturation between the groups. Patients experienced a comfortable surgical experience without immediate postoperative pain or any associated side effects.

VI. CONCLUSION

The addition of nalbuphine (10 mg) as an adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block in patients undergoing forearm and hand surgeries has been found to extend the duration of analgesia without any adverse effects. Moreover, the utilization of ultrasound guidance during the procedure eliminated any instances of technique-related complications. These findings suggest that nalbuphine could potentially be considered as an additional option among the growing list of adjuvants to local anesthetics.

REFERENCE

- Gupta K, Jain M, Gupta PK, Rastogi B, Zuberi A, Pandey MN. Nalbuphine As An Adjuvant To 0.5% Bupivacaine For Ultrasound-Guided Supraclavicular Brachial Plexus Blockade. Indian J Pain. 2016;30:176-80.
- [2]. Jarbo K, Batra YK, Panda NB. Brachial Plexus Block With Midazolam And Bupivacaine Improves Analgesia. Can J Anaesth. 2005;52:822-26.
- [3]. Fisher L, Gordon M. Anesthesia For Hand Surgery. In: Wolfe SW, Hotchkiss RN, Pederson WC, Kozin SH, Editors. 6a Ed. Churchill Livingstone/Elsevier; Philadelphia: 2010. Pp. 25-38. (Green's Operative Hand Surgery).
- [4]. Neal JM, Gerancher JC, Hebl JR, Ilfeld BM, Mccartney CJ, Franco CD, Et Al.Upper Extremity Regional Anesthesia: Essentials Of Our Current Understanding, 2008. Reg Anesth Pain Med. 2009;34:134-70.
- [5]. Tran QH, Clemente A, Doan J, Finlayson RJ. Brachial Plexus Blocks: A Review Of Approaches And Techniques. Can J Anaesth. 2007;54:662-74.
- [6]. Förster JG, Rosenberg PH. Clinically Useful Adjuvants In Regional Anaesthesia. Curr Opin Anaesthesiol 2003;16:477-86.
- [7]. Hadzic, A., Arliss, J., Kerimoglu, B., Karaca, P.E., Yufa, M., Claudio, R.E., Et Al. (2004) A Comparison Of Infractavicular Nerve Block Versus General Anesthesia For Hand And Wrist Day-Case Surgeries. Anesthesiology, 101, 127-132.
- [8]. Gunion MW, Marchionne AM, Anderson TM. Use Of The Mixed Agonist-Antagonist Nalbuphine In Opioid Based Analgesia. Acute Pain 2004;6:29-39.
- [9]. Perlas A, Lobo G, Lo N, Brull R, Chan VW, Karkhanis R. Ultrasound-Guided Supraclavicular Block: Outcome Of 510 Consecutive Cases. Reg Anesth Pain Med 2009;34:171-6.
- [10]. Cline E, Franz D, Polley RD, Maye J, Burkard J, Pellegrini J. Analgesia And Effectiveness Of Levobupivacaine Compared With Ropivacaine In Patients Undergoing An Axillary Brachial Plexus Block. AANA J 2004;72:339-45.
- [11]. Sáinz López J, Prat Vallribera A, Seguí Pericas M, Samà Pujolar A, Calleja Abad M, Sabater Recolons J, Et Al. Ultrasound-Guided Supraclavicular Brachial Plexus Block With Small Volumes Of Local Anesthetic: Technical Description And Analysis Of Results. Rev Esp Anestesiol Reanim 2006;53:400-7.
- [12]. Kaabachi O, Ouezini R, Koubaa W, Ghrab B, Zargouni A, Ben Abdelaziz A. Tramadol As An Adjuvant To Lidocaine For Axillary Brachial Plexus Block. Anesth Analg 2009;108:367-70.
- [13]. 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. Adv Biomed Res 2015;4:232.
- [14]. Young WS 3rd, Wamsley JK, Zarbin MA, Kuhar MJ. Opioid Receptors Undergo Axonal Flow. Science 1980;210:76-8.
 [15] Loudron PM. Avonal Transport Of Opioto Resentant In Conscision Specific Neuronal Processing Processing Specific Neuronal Processing Procesing Processing Processing Processing
- [15]. Laudren PM. Axonal Transport Of Opiate Receptors In Capsaicin-Sensitive Neurons. Brain Res 1984;68:413.
- [16]. Acharya R, Jena M, Mishra S, Rath SK. Effect Of Butorphanol Versus Placebo As Adjuvant To Bupivacaine For Supraclavicular Brachial Plexus Blockade. Int J Appl Pharm 2014;6:8-10.
- [17]. Viel EJ, Eledjam JJ, De La Coussaye JE, D'Athis F. Brachial Plexus Block With Opioids For Postoperative Pain Relief: Comparison Between Buprenorphine And Morphine. Reg Anesth 1989;14:274-8.
- [18]. Youssef MM, Elzayyat NS. Lidocaine-Nalbuphine Versus Lidocaine-Tramadol For Intravenous Regional Anesthesia. Ain Shams J Anaesthesiol 2014;7:198-204.
- [19]. Abdelhaq MM, Elramely MA. Effect Of Nalbuphine As Adjuvant To Bupivacaine For Ultrasound-Guided Supraclavicular Brachial Plexus Block. Open J Anesthesiol 2016;6:20-6.
- [20]. Chiruvella S, Konkyana SK, Nallam SR, Sateesh G. Postoperative Analgesia With Epidural Dexmedetomidine Compared With Clonidine Following Total Abdominal Hysterectomies: A Prospective Double-Blind Randomized Trial. Anesth Essays Res. 2018;12:135-39