ORIGINAL RESEARCH

The Analgesic Effect Of Nalbuphine As An Adjuvant To 0.5% Ropivacaine For Post Operative Analgesia In Ultrasound Guided Supraclavicular Brachial Plexus Nerve Blocks

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Abstract
Introduction: Nalbuphine a newer synthetic anta opioid with ceiling effect on respiratory depression establishing its efficacy in prolongation and effectiveness in regional block anaesthesia as an adjuvant with local anaesthetic drugs. The aim of this study was to evaluate the effect of nalbuphine in prolongation of duration of post-operative analgesia when it is added as an adjuvant to ropivacaine a local anaesthetic drug in ultrasound guided supraclavicular brachial plexus blocks. **Methodology:** A prospective randomized double blinded controlled interventional study was carried out to evaluate the effect of nalbuphine10mg as an adjuvant to 0.5% ropivacaine 20ml for post operative analgesia in USG guided supraclavicular BPB in patients undergoing upper limb surgeries. 64 patients of either sex aged 20 to 50yrs and physical status ASA grade 1and 2 were allocated randomly into two groups N and R of 32 each. In group N test group patients were given 20ml of 0.5% Ropivacaine and 10mg of Nalbuphine as an adjuvant while in group R control group patients were given 20ml of 0.5% Ropivacaine and 1ml of normal saline . The outcome and comparison were done in terms of onset and duration of sensory and motor block duration of analgesia and complications if any. **Results:** Both groups were demographically comparable. The mean onset of sensory block in Group N is 4.78 in 2.24min and in Group R is 5.34 in1.73min that is statistically significant p 0.01857. The mean onset of motor block in Group N is 7.56 in 1.72min and in Group R is 8.72 in 2.72min that is statistically significant p 0.02308. The mean Duration of Sensory Block in Group N was 425.34 in 10.37 min and in Group R was 261.59 in 9.01 min that was statistically highly significant p 0.000001.The mean Duration of Motor Block in Group N was 408.25 in 12.06 min and in Group R was 250.78 in 6.41 min that was statistically highly significant p 0.000001.The mean Duration of Analgesia in Group N was 435 in 12.20 min and in Group R was 274.34 in 55.46 min that was statistically highly significant p 0.000001. no complications were noted in both study groups. **Conclusion:** Nalbuphine as an adjuvant to Ropivacaine provides comparable results in term of decreasing the duration of onset of sensory and motor block and prolonging the duration of analgesia when compared to ropivacaine alone in USG guided supraclavicular brachial plexus nerve blocks.

Keywords: Analgesia, Brachial plexus nerve block ,Nulbuphine ,Ropivacaine ,Supraclavicular, Ultrasound

Introduction

Pain is an important issue to be addressed by an anaesthesiologist. Effective pain management leads to shortened hospital stay , earlier mobility and recovery along with reduced risk of deep venous thrombosis, pulmonary and cardiac complications, hence increased patient satisfaction and reduced cost .Ropivacaine, an amide local anaesthetic, decreased potential for the central nervous system toxicity and cardiotoxicity due to reduced lipophilicity which provides wider safety margin,1,2 is very commonly used as local anaesthetic for supra clavicular brachial plexus nerve block. Combination of various adjuvants along with local anaesthetic drugs have been tried to extend the duration of analgesia during postoperative period in regional block anaesthesia. Opioid

administration as an adjuvant with local anaesthetic drugs prolongs analgesia effectively with very less incidence of local/systemic side effects. Nalbuphine, a mixed k-agonist-μ- antagonist opioid drug, attract attention of many anaesthesia practitioners now a days due to its reliable and effective results for prolongation of post operative analgesia as an adjuvant drug with local anaesthetics.Easy availability, low cost, and less side effects make it more suitable than other commonly used opioids as adjuvant with local anaesthetic drugs.3Newly emerging drug with less literature availability make it attractive research prospective to be studied. We conducted this study to evaluate the effect of nalbuphine in prolongation of duration of post-operative analgesiawhen it is added as an adjuvant to ropivacaine in performing ultrasound guided supraclavicular brachial plexus blocks. Our present study was undertaken to ascertain to prove the efficacy of Nalbuphine in prolongation of duration of post operative analgesia when it is added as an adjuvant to 0.5% Ropivacaine while performing ultrasound guided supraclavicular brachial plexus blocks.

Methods

This study was registered at the CLINICAL TRIAL REGISTRY INDIA on 24/06/2022 as CTRI/2022/06/043470 [Registered on: 24/06/2022] - Trial Registered Prospectively and approved by institutional ethics committee of SMS medical college, Jaipur on 01/12/21 as 1118/MC/EC/2021. This study adhered to the CONSORT guidelines and relevant institutional guidelines and government regulations as per norms. We used Sonosite M turbo point of care portable ultrasound scanner machine for USG guided block after getting permission from the regulatory authority in Trauma centre of SMS medical college, Jaipur, India. Seed article[4]for the study was-ORIGINAL ARTICLE P J M H S Vol. 14, NO. 2, APR – JUN 2020 1572 [Determine the Effectiveness of Nulbuphine with Ropivacaine in Supraclavicular Brachial Plexus Block].A Hospital based prospective randomized double blinded controlled interventional study for 9 months (Feb 2021-Oct 2021) was carried out with 64 patients(age between 20 to 50 yrsof either sex, ASA physical status class 1 & 2 and willing to participate) undergoing various types of upper limb surgeries under ultrasound guided supraclavicular nerve blocks anaesthesia. After getting ethics committee approval and written informed consent from patients, patient was registered for the study. 64 patients satisfying inclusion criteria were selected using simple random sampling on thebasis of patients first admitted. Eligible cases were be randomly allocated in two study groups by using opaque sealed envelope with replacement method. Patient was explained about the procedure but was not be aware about the type of drug. The anaesthesiologist who would administer the drugs, would be different from the anaesthesiologist who would collect data. The person keeping the record of the NRS score, Hollman's score and Modified bromage score and also other data inpost-operativeperiodwould be blindedto thegroups.64 patients were allocated randomly into two groups of 32 each. In group N (test group) patients were given 20ml of 0.5% Ropivacaine and 10mg(1ml) of Nalbuphine as adjuvant while in group R (control group) patients were given 20ml of 0.5% Ropivacaine and 1ml of normal saline . The evaluation and comparison was done in terms of onset and duration of motor and sensory block, duration of analgesia, hemodynamic changes and complications if any. Inclusion criteria for this study was patientsundergoingtraumaticorthopaedicforearmfractu resurgeriesundersupra clavicular brachial plexus block anaesthesia technique, ASA group 1 and 2 of either sex, age group 20yrs to 50yrs andwillingto participate. Patientswithahistoryofallergyorhypersensitivitytoeithe rlocalanaesthetic or drugs, Anycontraindication toperipheralnerveblock**,** Impaired ability to communicate(eg:confusion,poorhearing.orlanguageba rrier)PatientswithraisedICT(Intracranialtension)and Pregnancy were categorised as exclusion criteria.

Scales use for assessment of various block levels

HOLLMAN'S SCALE (for quality of Sensory block)

1. Grade 0 – normal sensation with pinprick.
2. Grade I – pinprick felt as sharp pointed but weaker compared with the same area of other side
3. Grade II – pinprick felt as touch with blunt object.
4. Grade III –no sensation of pinprick.

MODIFIED BROMAGE SCALE (for quality of motor block)

1. Grade 0– No block, total arm and forearm flexion.
2. Grade I – Partial block, total forearm and partial arm flexion.
3. Grade II – Almost complete block, inability to flex the arm and decreased ability to flex the forearm.
4. Grade III – Total block, inability to flex both arm and forearm.

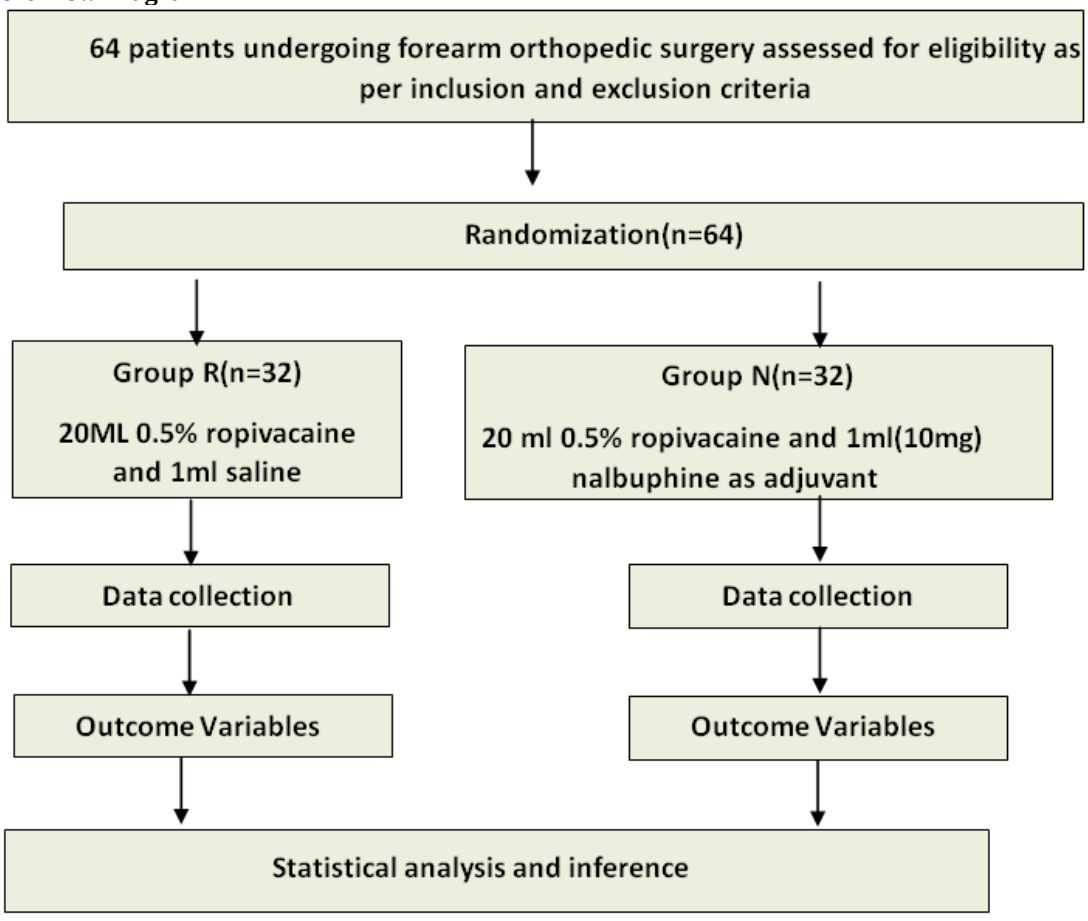
NUMERIC RATING PAIN SCALE (for quality of analgesia)

1. Score 0– No pain.
2. Score 1,2,3 –Mild pain.
3. Score 4,5,6 –Moderate pain.
4. Score 7,8,9 –Severe pain.
5. Score 10 -Worst imaginable pain.

Anaesthesia and perioperative treatment: All patients were visited on the day prior to surgery and explained about the anaesthetic technique, drugs effect/side effects and perioperative course and well informed written consent was taken. On operation day, fasting & NBM status, written informed consent

and pre anesthetic checkup findings would be confirmed. Hollman's score, Modified bromage score and NRS score were explained to all candidates in their vernacular language. Baseline parameter monitoring was started to record – For blood pressure - atevery5 mininterval for the first 30 min and 15min interval therafter and for ECG and SPO2 - continueous monitoring till the completion of surgery. We placed the patient in supine position and turned the patient's head to 45degrees to the opposite side of the block. An Sonosite M turbo point of care portable ultrasound scanner Ultrasound machine were used. Under All aseptic precautions, probe preparation was done. The skin is first cleaned and draped. Scanning was done from midline to supraclavicular fossa, identifying the subclavian artery, resting on 1st rib the plexus lies lateral to subclavian artery. The brachial plexus was identified as bunch of grapes. A block was performed by out ofplane technique. In order to block lower trunk, 5ml of drug was injected in the corner pocket and the remaining volume was injected around the nerve plexus. In order to preventany IV injection, repeated aspiration were done and low alliquates of drug were given. After the USG-guided anesthetic drug administration, onset of blockwas accessed by pin prick method at every 2 min till onset of block. For sensory block , we achieved grade 3 (no sensation on pin prick) on Hollman's scale before starting surgery. For motor block, we achieved Modified bromage scale Grade 3 (total block, inability to flex both arm and forearm) before starting surgery. Intraoperative, the patient's heart rate, mean arterial pressure was noted down at every 5 minutes during the first 30 min then at every 15min till the end of the surgery. If sensory or motor blockade was inadequate even after 30 minutes of administration of USG–guided anesthetic drug,it would be taken as an unsuccessful block. Onset of sensory/motor block was the time period between drug administration and onset of drug effect. The sensory block was assessed by pin prick method and motor block was assessed as per modified bromage scale after stabilization of the fracture. Duration of sensory/motor block was the time period between block onset and return of sensory/motor effect. Duration of analgesia was the time period between onset of analgesia and complain of pain at the level of NRS scale grade 4. Tramadol 1mg/kg was used for first rescue analgesia at NRS>4 numeric scale in the postoperative period.

Consort Flow Diagram



A sample size of 64 cases was calculated using duration of analgesia as primary outcome in each group which was adequate at 95% Confidence and80% power to verify the expected difference of 262(±22.43) minutes in mean duration of analgesiain both study groups, as per the seed article. Data were

entered into Microsoft Excel spreadsheet and analyzed using SPSS Statistics-26 version to draw relevant conclusions. The observations were tabulated in the form of mean ± standard deviation (SD). For parametric data, Student's paired "t" test was applied. Categorical variables were correlated using chi-square test. The level of significance was determined as "p" value with $p < 0.05$ as significant and $p < 0.001$ as highly significant.

Results

Table 1: Descriptive statistics of Onset of Sensory Block

Parameters	Minimum	Maximum	Median (IQR)	Mean ± SD	P value
Onset of Sensory Block For Group N(min)	3	8	4 (3 , 5)	4.78 ± 2.24	p=0.01857
Onset of Sensory Block For Group R(min)	3	10	5 (3 , 6)	5.34 ± 1.73	

The mean onset of sensory block in Group N is 4.78 ± 2.24min and in Group R is 5.34 ± 1.73min that is statistically significant (p=0.01857).
It shows reduction in time of onset of Sensory block in nalbuphine adjuvant group.

Table 2: Descriptive statistics of Onset of Motor Block

Parameters	Minimum	Maximum	Median (IQR)	Mean ± SD	P value
Onset of Motor Block For Group N(min)	5	10	7 (6.75 , 9.25)	7.56 ± 1.72	p=0.02308
Onset of Motor Block For Group R(min)	4	16	8 (7 , 12)	8.72 ± 2.72	

The mean onset of motor block in Group N is 7.56 ± 1.72min and in Group R is 8.72 ± 2.72min that is statistically significant (p=0.02308). It shows reduction in time of Onset of Motor block in nalbuphine adjuvant group.

Table 3: Descriptive statistics of Duration of Sensory Block

Parameters	Minimum	Maximum	Median (IQR)	Mean ± SD	P value
Duration of Sensory Block of Group N(min)	406	442	426 (418.5 , 433)	425.34 ± 10.37	p=0.000001
Duration of Sensory Block of Group R(min)	245	273	265 (253.5 , 270)	261.59 ± 9.01	

The mean Duration of Sensory Block in Group N is 425.34 ± 10.37 min and in Group R is 261.59 ± 9.01 min that is statistically highly significant (p=0.000001).So the Duration of Sensory block is significantly increased in nalbuphine adjuvant group.

Table 4: Descriptive statistics of Duration of Motor Block

Parameters	Minimum	Maximum	Median (IQR)	Mean ± SD
Duration of Motor Block of Group N(min)	387	429	409 (398 , 417.75)	408.25 ± 12.06
Duration of Motor Block of Group R(min)	240	260	252 (244 , 257)	250.78 ± 6.41

The mean Duration of Motor Block in Group N is 408.25 ± 12.06 min and in Group R is 250.78 ± 6.41 min that is statistically highly significant (p=0.000001). So the Duration of Motor block is significantly increased in nalbuphine adjuvant group.

Table 5: Descriptive statistics of Duration of Analgesia

Parameters	Minimum	Maximum	Median (IQR)	Mean ± SD	P value
Duration of Analgesia For Group N (min)	410	455	436 (426 , 443)	435 ± 12.20	p=0.000001
Duration of Analgesia For Group R (min)	181	365	278.5(230.5,322.75)	274.34 ± 55.46	

The mean Duration of Analgesia in Group N is 435 ± 12.20 min and in Group R is 274.34 ± 55.46 min that is statistically highly significant (p=0.000001). So the Duration of Analgesia is significantly increased in nalbuphine adjuvant group.

Table 6: Perioperative block characteristics in each group

Groups	Group N Mean±SD(min)	Group R Mean ±SD(min)	P-Value	Significance
Onset of Sensory Block	4.78 ±2.24	5.34 ±1.73	p=0.01857	Significant
Onset of Motor Block	7.56 ± 1.72	8.72 ± 2.72	p=0.02308	Significant
Duration of Sensory Block	425.34±10.37	261.59±9.01	p=0.000001	Highly significant
Duration of Motor Block	408.25 ± 12.06	250.78 ± 6.41	p=0.000001	Highly significant
Duration of Analgesia	435 ± 12.20	274.34 ±55.46	p=0.000001	Highly significant

In the present study, 64 patients who met the inclusion criteria were assessed and randomized for the study (Flowchart 1). Demographic data including age, sex, weight, ASA classification were comparable statistically .In Nalbuphine adjuvant group (Group N/test group), Duration of analgesia was significantly increased than group R(Ropivacaine only group/control group). Onset of sensory and motor block were also significantly reduced in Nalbuphine adjuvant group(Group N/test group) compared to group R(Ropivacaine only group/control group). Duration of sensory and motor block was also significantly increased in Nalbuphine adjuvant group(Group N/test group) compared to group R(Ropivacaine only group/control group).

The intraoperative block characteristics showed a rapid onset of both motor and sensory block in group N as compared to group R. Even the duration of motor and sensory block in group N was highly significant compared to group R.All patients remained hemodynamically stable in both the groups during the intraoperative and postoperative period as assessed by mean heart rate and mean arterial pressure (MAP).No complication and no block failure was recorded in our study.

Discussion

In our study, we found that the onset time of sensory and motor block was faster inthenalbuphine adjuvant groupascomparedtoplainropivacainegroupandshoweds tatisticallysignificant difference(P<0.05).Nalbuphine is a mixed k-agonist-μ-antagonist opioid with a moderate analgesic effect when compared to morphine. Its affinity to k-opioid receptors results in analgesia, sedation, and cardiovascular stability with minimal respiratory depression. There is a great similarity between butorphanol and nalbuphine regarding the chemical nature (synthetic mixed k-agonist-μ-antagonists), also, both have the same mode of action on opioid receptors, and inhibition of neuronal serotonin uptake which leads to augmentation of the spinal inhibitory pathways for pain13. Stimulation of opiate receptors on neurons of the central nervous system lead to an inhibition of intracellular adenylyl cyclase, an opening of potassium channels, and closing the calcium channels. This leads to hyperpolarization of the cell membrane potential and inhibition of action potential transmission of ascending pain pathways.11Priti jadejaet al7found very similar results to our study. Her study was Comparative Evaluation of Ropivacaine Alone with Ropivacaine Nalbuphine Combination in Supraclavicular Brachial Plexus Block for Upper Limb Surgery.Guptaet al6and Das et al8also assessed the analgesic efficacy of 10 mg nalbuphineas an adjuvant to bupivacaine and levobupivacaine, respectively, for brachial plexusblock and found comparable results in both groups regarding onset of block (P >0.05)However, in contrast, Nazir and Jain9observed statistically significant shorter time to onset of sensory and motor blockade using 30 mL of 0.375% bupivacaine with 10 mgnalbuphine. Our study demonstrated Highly significant longer duration of sensory and motorblockas well asduration of analgesia in nalbuphine group. Similar findings were observed by Abdelhaq and Elramely, Gupta et al., Das et al.,and Nazir and Jain in their studies5,6,8,9. These studies were in accordance toour results, showing addition of nalbuphine to LAs increases the duration of block and analgesia.

Nalbuphineis not associated with any hemodynamic variabilityoranyadverseevent.Asnalbuphineisagonistto κreceptorandantagonisttoμreceptors, it is devoid of pruritus, nausea, vomiting, and respiratory depression. The intraoperative changes in vital parameters and oxygen saturation showed insignificant difference between the groups during the present study. Patients were comfortable due to painless performance and no immediate postoperative pain or side effects. The difference in the duration in various studies can be explained by the difference in the strength and volumes of drug used in these studies. Probable explanation for all this inconsistency in various studies regarding onset and duration may relate to inter patient variations in the study population, anatomy of the plexus sheath & difference in the spread of local anaesthetics in the plexus sheath depending upon the block technique .There are reported differences in the effects of administration of Nalbuphine on timeof onset and efficacy of nerve blocks which may be explained by differences in the type of drug, type of nerve block, concentration of drug, exact volume of mixture injected and technique used to perform block. Also the technique varies with studies ranging from

paraesthesia to echo guided blocks. The varied results may be because sometimes drug is not able to penetrate layers of axonal myelin. It is also possible that the prepared local anaesthetic and nalbuphine solutions may alter the quantity and onset of block by changes in pH of the solution. Different study designs, the use of different local anaesthetics with nalbuphine, the different site of block (axillary. supraclavicular, inter scalene), addition or omission of adjuvant may be other reasons for such varied results. The time of onset of block depends on many factors such as lipid solubility and pK a of drug, fraction of nonionized drug (depends on pH of solution and surrounding medium), and nerve fiber size. In our study, we did not measure the pH of solution after mixing of nalbuphine with ropivacaine. In our study the onset time of sensory and motor block was faster in the nalbuphine adjuvant group as compared to plain ropivacaine group that help to reduce pain .There were some limitations of our study that single dose of nalbuphine and LA i.e., single-shot PNB (sPNB) was used which could not provide long-term benefit to the patient as evidence suggested that continuous PNBs offer advantages over sPNBs, including a longer duration of analgesia and are indicated mainly for perioperative analgesia. Although assessment of pain by NRS is simple, it is highly subjective as all the patients had dissimilar pain tolerances and various patients misunderstood how to use it properly and patients sometimes needed specific instructions during their pain assessment which may have caused bias in our results

Conclusion

The study concludes that Nalbuphine as an adjuvant to Ropivacaine provides comparable results in term of decreasing the duration of onset of sensory and motor block and prolonging the duration of analgesia when compared to ropivacaine alone in USG guided supraclavicular brachial plexus nerve blocks.

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