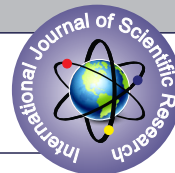


COMPARATIVE STUDY TO EVALUATE THE EFFECT OF FENTANYL, CLONIDINE AND NALBUPHINE AS AN ADJUVANT TO 0.5% ROPIVACAINE ON SENSORY BLOCKADE, MOTOR BLOCKADE & POSTOPERATIVE ANALGESIA IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCKADE



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ABSTRACT

Introduction: The supraclavicular block is most easily executable and consistent method for anaesthesia for upper limb surgeries. An extended range of adjuvants have been combined with local anaesthetics and have demonstrated very encouraging outcomes in clinical practice. **Aims And Objectives:** The aim of this study was to evaluate the onset, duration of sensory and motor block, hemodynamic effect (if any), duration of postoperative analgesia, and adverse effect of fentanyl, clonidine and nalbuphine when used as an adjuvant to 0.5 % ropivacaine in patient undergoing upper limb orthopaedic surgeries in supraclavicular block. **Material And Methods:** this prospective randomised single blind comparative study was conducted in total 90 patients undergoing upper limb orthopaedic surgery, divided into three groups of 30 patients each. Group C received 30 ml of 0.5% ropivacaine with 1 µg /kg Clonidine, Group F received 30 ml of 0.5% ropivacaine with 1 µg /kg Fentanyl and Group N received 30 ml of 0.5% ropivacaine with 0.3 mg/kg Nalbuphine. The onset and duration of sensory and motor blockade, duration of postoperative analgesia, hemodynamics and side effects were observed. **Results & Conclusion:** The mean time of onset of sensory and motor block was less in clonidine group ($P < 0.0001$). Duration of motor block was more in clonidine group ($P < 0.0001$). Duration of sensory block and duration of post operative analgesia was more in Nalbuphine group ($P < 0.0001$). Whereas no significant side effects were observed in any of the groups. Our study concluded that nalbuphine, clonidine and fentanyl were good adjuvants to ropivacaine in supraclavicular block. Addition of clonidine fastens the onset of sensory and motor blockade and also prolongs the duration of motor blockade, whereas addition of Nalbuphine prolongs duration of sensory blockade and postoperative analgesia.

KEYWORDS

supraclavicular block, fentanyl, nalbuphine , clonidine

INTRODUCTION

The most popular method for doing upper limb procedures is brachial plexus block⁽¹⁾ which can be used instead of or in addition to general anaesthesia to provide appropriate muscular relaxation, maintain intraoperative hemodynamic stability, and sympathetic block.⁽²⁾ The upper limb blocks mainly avoid the consequences of general anaesthesia like polypharmacy, pressor response to laryngoscopy etc.⁽³⁾

Ropivacaine is one of the most commonly used amide local anaesthetic for supraclavicular block as it is less cardiotoxic as compared to other amide local anaesthetics. However, it has restrictions such as like delayed onset and poor motor blockade.⁽⁵⁾

An extended range of adjuvants are used in supraclavicular block in upper limb procedures to address the downside of delayed onset on sensory blockade, motor blockade and shorter duration of postoperative analgesia, and have demonstrated very encouraging outcomes in clinical practice.⁽⁶⁾

Fentanyl a synthetic opioid and μ receptor agonist, is a highly lipid soluble drug has been successfully used as adjuvants to local anaesthetics in brachial plexus block due to their rapid onset, and prolonged analgesia, possible mechanism of direct action on peripheral opioid receptors.⁽⁷⁾

Clonidine, an imidazoline is a selective α -2 adrenergic agonist with certain α -1 agonist properties.⁽⁸⁾ Adjuvant administration of α -2 adrenergic agonist drugs to local anaesthetics improves their action via local α -2 mediated vasoconstriction and facilitation of C fibre blockade.⁽⁹⁾

Nalbuphine, a derivative of 14-hydroxymorphine, is an agonist antagonist opioid acting on μ (μ) receptors as antagonists and κ (κ) receptors as agonists.⁽¹⁰⁾ Nalbuphine has also gained prominence in pain management; nevertheless, its effectiveness as a local anaesthetic adjuvant in peripheral nerve blockades has not yet been established.⁽¹¹⁾

Therefore, in the present study, we compared the efficacy of fentanyl, clonidine and nalbuphine with ropivacaine on onset and duration of sensory and motor block with requirement of analgesia in supraclavicular brachial plexus block.

Aims And Objectives

The aim of this study was to compare the block characteristics between clonidine, fentanyl and nalbuphine when used as an adjuvant to 0.5% ropivacaine in supraclavicular brachial plexus block.

The Objectives Of This Study Were As Follows:

1. The time of onset of sensory blockade
2. The time of onset of motor blockade
3. The duration of sensory blockade
4. The duration of motor blockade
5. The duration of analgesia and intra and post operative visual analogue scale (VAS) scores
6. Incidence of side effects if any

MATERIAL AND METHODS

The study was randomised controlled trial conducted on ninety patients between 18-60 years of age with ASA physical grade I and II posted for elective upper limb orthopaedic surgeries under supraclavicular block. After obtaining approval from ethical committee 90 patients who fulfil the eligibility criteria were chosen, explained about the procedure and written consent was taken. Patient were subsequent randomized into three groups of 30 each namely Group RF, Group RC and Group RN using slips in the box technique.

Grouping: 90 Patients Were Randomly Divided Into 3 Groups:

Group RF (n=30) - 30 ml of 0.5% ropivacaine with 1 µg /kg Fentanyl

Group RC (n=30) - 30 ml of 0.5% ropivacaine with 1 µg /kg Clonidine

Group RN (n=30) - 30 ml of 0.5% ropivacaine with 0.3 mg/kg Nalbuphine

Inclusion Criteria:

- 90 patients of ASA grade I and II.

- Male and non-pregnant females of age group - 18-60 yr

Exclusion Criteria:

- Following patient was excluded in the study:
- Age < 18 yr or > 60 yrs.
- History of allergy or sensitivity or any other reaction to local anaesthetics.
- Hypertensive patient on treatment with beta blocker, methyl dopa, MAO inhibitor, tricyclic antidepressants.
- History of significant neurological, psychiatric or neuromuscular disorder.
- Renal dysfunction Cardiac disease
- Patient with elevated AST, ALT values.
- Parturient and lactating women
- History of bleeding disorder

After patient's arrival in the operating room 18G IV cannula is inserted, RL solution will be started @ 10-15 drops/min and placed at the forearm contralateral to the arm to be operated and Inj. Glycopyrrrolate 0.005-0.01 mg/kg half hour before surgery premedication is to be given I/V standard monitoring will be used throughout the procedure including NIBP, HR, pulse oximeter.

Procedure:

Supraclavicular block classical approach (nerve stimulator technique), patient was placed in dorsal recumbent position without a pillow, arms by the side, and head turned (30-45°) towards the opposite side to be blocked. Small pillow/sand bag/towel folded was placed below shoulder blades for adequate positioning. The patient was instructed to lower his shoulder and supinate his arm. The neck and the shoulder were painted and draped. The operator stood on the side to be blocked, the palpation is done with left hand and needle is manipulated with right hand. The sternocleidomastoid (SCM) posterior border was identified and followed distally to the clavicle. The point of needle entry is about one inch lateral to insertion of SCM or one thumb breadth lateral to SCM. Palpation of the subclavian artery at the site confirms the landmark. The palpating index finger was placed at this site. Local infiltration of 1ml of 2% Lignocaine is given. This technique was carried out using an insulated needle. The needle is connected to nerve stimulator by electrodes, and is properly grounded with the help of ECG lead. The stimulation was started with intensity of 2.0mA and pulse duration of 0.1 milliseconds and frequency of 2 Hertz. Once the desired response was obtained that is a muscle twitch of the fingers current was gradually reduced to 0.6mA. If the response was obtained even with 0.4mA also, then the needle was repositioned again so as to get response to 0.6mA and not 0.4mA. If adequate response was not obtained, needle was withdrawn a penetration angle was adjusted in the antero-posterior plane. Wrist flexion and extension of fingers is taken as acceptable responses. Total volume of the anesthetic solution was injected at an incremental dose of 5ml each, preceded by negative aspiration, 3-minute massage was performed to facilitate even drug distribution. The onset of sensory block was evaluated using 3 point scale (0- Normal sensation, 1- reduced sensation, 2- absent). Onset of motor block was assessed by 4-point scale (0- no paralysis, 1-shoulder abduction, 2-elbow flexion, 3- wrist flexion, and 4- complete block). When complete anaesthesia was achieved, the surgery was allowed to proceed. Total duration of analgesia was taken from the time of complete sensory block to the request of rescue analgesic VAS ≥ 3 .

Interventions And Observations:

- 1) Onset Of Sensory Block:** was defined as the time taken from the completion of the injection of study drug, till the time that the patient did not feel the pin prick at elbow level. Surgical incision was commenced when sensory blockade was adequate in all dermatomes. If the block was inadequate then the patient was given general anaesthesia and was excluded from the study.
- 2) Onset Of Motor Block:** Defined as the time consumed from injection of drug to complete motor block. Motor block is evaluated by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of the elbow in supination and pronation of the forearm (musculocutaneous nerve).
- 3) Duration Of Motor Block:** Time consumed between injection of the drug to complete return of motor power.
- 4) Assessment Of Postoperative Pain and Duration of Sensory Block:** Postoperative Pain is assessed using a visual analogue score scale which consisted of a 10 cm horizontal scale with

gradations marked as 0 means no pain at all and 10 means unbearable pain.

VAS score is recorded every 60 min in the postoperative period till the conclusion of study. It refers to the period of time between the onset of the brachial plexus block and the first dose of rescue analgesic that the patient required i.e., VAS score >3 was managed with rescue analgesia with Inj. Tramadol 2 mg/kg IV in 100 ml normal saline to relieve postoperative pain.

OBSERVATION AND RESULTS

Study Design

Comparative study to evaluate the effect of fentanyl, clonidine and nalbuphine as an adjuvant to 0.5% ropivacaine on sensory blockade, motor blockade & postoperative analgesia in supraclavicular brachial plexus blockade

Table 1: Demographic Variable

	Clonidine	Fentanyl	Nalbuphine	Total	p-value
Mean Age (yrs)	36.9±11.32	43.77±12.69	42.1±9.35	40.93±11.46	0.051
Mean weight (kg)	60.40±6.17	59.3±5.77	60.27±6.16	59.63±5.85	0.744
Gender (M/F)	13/17	15/15	16/14	44/46	0.732

Above table shows that the demographic profile of the three groups were comparable as p value is >0.05 which is statistically not significant.

Table 2: Onset Of Sensory Block

	Clonidine (RC)	Fentanyl (RF)	Nalbuphine (RN)	Total	F-value	p-value
Onset of sensory block (minutes)	4.4±0.83	11.25±1.23	8.85±1.25	8.17±3.07	291.266	<0.0001

The above table shows Onset of sensory block in the study groups, the onset of sensory block was found to be 4.4±0.83 mins in group RC, 11.25±1.23 mins in group RF and 8.85±1.25 mins in group RN with a p value of (p= <0.0001) which is statistically highly significant meaning that the group RC has the fastest onset of sensory block followed by nalbuphine group and longest time for onset of sensory block was observed in RF group.

Table 3: Onset Of Motor Block

	Clonidine (RC)	Fentanyl (RF)	Nalbuphine (RN)	Total	F-value	p-value
Onset of motor block (minutes)	9.24±1.44	16.19±1.65	14.72±1.05	13.38±0.32	206.030	<0.0001

The above table shows Onset of Motor block in the study groups, the onset of motor block was found to be 9.24±1.44mins in group C, 16.19±1.65mins in group F and 14.72±1.05mins in group N with a p value of (p= <0.0001) which is statistically highly significant meaning that the group C has the fastest onset of motor block followed by nalbuphine group and longest time for onset of motor block was observed in Fentanyl group.

Table 4: Duration Of Sensory Block

	Clonidine (RC)	Fentanyl (RF)	Nalbuphine (RN)	Total	F-value	p-value
Duration of sensory block (minutes)	706.44±74.76	549.34±28.76	724.6±21.48	660.13±92.21	121.561	<0.0001

The above table shows mean duration of Sensory block in the study groups, the duration of sensory block was found to be 706.44±74.76mins in group C, 549.34±28.76 mins in group F and 724.6±21.48in group N with a p value of (p= <0.0001) which is statistically highly significant meaning that the group N has the longest duration of sensory block followed by clonidine group and shortest duration was observed in Fentanyl group.

Table 5: Duration Of Motor Block

	Clonidine	Fentanyl	Nalbuphine	Total	F-value	p-value
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Duration of motor block (minutes)	642.34±33.71	519.67±44.45	414.07±12.47	525.36±99.32	359.30	<0.0001
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The above table shows Duration of Motor block in the study groups, the duration of motor block was found to be 642.34±33.71mins in group C, 519.67±44.45mins in group F and 414.07±12.47 mins in group N with a p value of (p= <0.0001) which is statistically highly significant meaning that the group C has the longest duration of motor block followed by Fentanyl group and shortest duration of motor block was observed in Nalbuphine group.

Table 6: Time For Rescue Analgesia (in Minutes) In Different Groups

	Clonidine	Fentanyl	Nalbuphine	Total	p-value
Time for rescue analgesia (minutes)	619.67±58.34	530.33±24.3	715.1±11.07	669.48±63.64	<0.0001

Above table shows delayed requirement of analgesia in Nalbuphine group (715.1±11.07 min), as compared to Clonidine group (619.67±58.34mins), earliest requirement of rescue analgesia was seen in fentanyl group (530.33±24.3 min). The difference was statistically highly significant (p value <0.0001). Nalbuphine provides longer duration of post operative analgesia as compared to clonidine, least duration of analgesia in our present study was seen in fentanyl group.

DISCUSSION

Supraclavicular brachial plexus block is preferred for its rapid onset, reliable anaesthesia and as a safe technique for any surgery in the upper extremity that does not involve the shoulder.⁽¹²⁾ This is because the block is performed at the level of nerve trunks, where, almost the entire innervations of the upper extremity are confined to a very small surface area.⁽¹²⁾ Brachial plexus block is usually performed using a mixture of local anaesthetics. Ropivacaine is a pure S (-) enantiomer, structurally related to bupivacaine, developed for the purpose of reducing potential toxicity and improving relative sensory and motor block profiles.⁶⁶ The efficacy of ropivacaine is similar to that of bupivacaine and levobupivacaine for peripheral nerve blocks. Ropivacaine with its efficacy, lower propensity for motor block and reduced potential for cardiotoxicity and central nervous system toxicity, appears to be an important option for regional anaesthesia and management of postoperative pain.⁽¹³⁾ But however, it has the disadvantage of patchy and incomplete analgesia. In order to overcome this disadvantage various adjuvant drugs have been used to make it more effective for surgery and postoperative analgesia.

Anaesthesia of entire upper extremity and perioperative analgesia are provided by supraclavicular brachial plexus block in an easy way without any systemic side effects. While catheter-based techniques allow for sustained pain management during the peri-operative period, they can present challenges related to patient management, catheter displacement, and increased infection risk.⁽¹⁴⁾ Hence, using adjuvant to local anaesthetics is a better and safer option to prolong the analgesia. Alpha-2 agonists have analgesic, anxiolytic, sedative, and sympatholytic properties, which make it a better choice for local anesthetic.⁽¹⁵⁾ The addition of clonidine or fentanyl to local anaesthetics produces analgesia, sedation with minimal side effects. Their use is established as onset is rapid with prolonged analgesia.⁽¹⁶⁾

Nalbuphine is a mixed kappa agonist and mu antagonist opioid. Its analgesic and sedative action is due to its affinity to kappa receptors. It has cardiovascular stability; unlike other opioids it has ceiling effect on respiratory depression. Opioids penetrate the nerve membrane, act at the dorsal horn, and increase the circulating endorphins.

Our present study consisted of 90 patients in the age group 18-60 years belonging to ASA grade 1 and 2 and were randomly divided into three groups (n=30 each). Group RC received 30 ml of 0.5% ropivacaine with 1 mcg/kg clonidine, group RF received 30 ml 0.5 % ropivacaine with 1 mcg/kg fentanyl and group RN received 30 ml 0.5 % ropivacaine with 0.3 mg/kg nalbuphine.

Demographic Characteristic

In our present study, we had enrolled 90 patients and randomly divide them in 3 groups namely group RC, group RF and group RN. The demographic characteristics in our study groups such as age, weight, and gender wise distribution (Table no 1) shows that they are

comparable at baseline as p value is >0.05. In accordance with our study **Kumar R. et al**⁽¹⁷⁾ also observed no significant difference in demographic variables. **Kangad S. et al**⁽¹⁸⁾ also found no significant difference in baseline demographic variables in the study groups.

Onset of Sensory Block (Table no. 2)

In the present study, mean time of onset of sensory block was 4.4±0.83 mins in group RC, 11.25±1.23 mins in group RF and 8.85±1.25 mins in group RN with p value <0.0001 meaning the difference between the groups are statistically highly significant meaning that the earliest onset of sensory block was seen in patients receiving clonidine followed by nalbuphine then fentanyl.

In study conducted by **Kumar R. et al**⁽¹⁷⁾ he evaluated efficacy of fentanyl and nalbuphine as an adjuvant to bupivacaine in supraclavicular block he found mean time of onset of sensory block to be 12.07±1.08 mins in fentanyl group and 8.20±1.32 mins in nalbuphine group showing early onset of sensory blockade in nalbuphine group as compared to fentanyl group. In a similar study conducted by **Naveen P. et al**⁽¹⁹⁾ he concluded that clonidine as an adjuvant to ropivacaine significantly shortens the onset of sensory blockade.

Contrary to findings of our current study **Puri A et al**⁽²⁰⁾ found that onset of sensory blockade was 13.17±2.45 mins in clonidine group and 8.43±2.89 mins in fentanyl group with p value <0.05 which is statistically significant.

Onset of Motor Block (Table no. 3)

In our present study we found that mean time of onset of motor blockade was 9.24±1.44 mins in group RC, 16.19±1.65 in group RF and 14.72±1.05 mins in group RN with p value <0.0001 which is statistically highly significant, meaning that fastest onset of motor blockade was seen in patient receiving clonidine followed by nalbuphine then fentanyl.

In accordance with our study **Kumar R. et al**⁽¹⁷⁾ also found that Group F had delayed onset of motor blockade (in minutes) compared to Group N. Also, according to study conducted by **Meena MR et al**⁽²¹⁾ they concluded that Group F had the delayed onset of sensory blockade (minutes) as compared to Group C.

Similarly, **Abdelhaq MM et al**⁽²²⁾ reported that the adding of 20 mg nalbuphine to bupivacaine in supraclavicular brachial plexus block results in early onset in motor block (17.4±1.14 minutes) as compared to control group.

Duration Of Sensory Block (Table no.4)

In the present study we found that mean duration of sensory block was 724.6±21.48 in group RN, 706.44±74.76 mins in group RC and 549.34±28.76 mins in group RF, showing longest duration of sensory blockade in patients receiving nalbuphine as compared to clonidine followed by fentanyl. The p value for above observation was found to be <0.0001 which is statistically highly significant.

Similarly, in study conducted by **Kumar R. et al**⁽¹⁷⁾ Group N had the longest duration of sensory block (minutes) compared to Group F. Contrary to our study **Meena MR. et al**⁽²¹⁾ found that Group C had the longest duration of sensory analgesia (minutes) compared to Group F.

Duration Of Motor Blockade (Table No. 5)

In the present study we observed that mean duration of motor block was found to be 642.34±33.71 mins in group RC, 519.67±44.45 in group RF and 414.07±12.47 in group RN, with p value <0.0001, which is statistically highly significant. Group C had longest duration of motor block (minutes) compared to Group F then Group N when added as adjuvant to ropivacaine for upper limb surgeries. According to **Meena MR. et al**⁽²¹⁾ study, Group C had the longest duration of motor block (minutes) compared to Group F. Contrary to our study results, **Kumar R. et al. study**⁽¹⁷⁾ was found that Group N had the highest duration of motor block (minutes) compared to Group F.

Time for Rescue Analgesia (Table no. 6)

In our present study we recorded VAS score in each of the three groups of patients every hourly from induction till 12 hours (Table no.6). we in our study observed that VAS score increases in each of the three groups with increase in time, we observed VAS score each hourly in all the three groups and gave rescue analgesia when the VAS score became 3,

we observed that higher VAS score was observed in group RF as compared to group RC then group RN, meaning longer duration of analgesia in nalbuphine group followed by clonidine group than fentanyl group. **Puri A. et al.**⁽²⁰⁾, **Naveen P. et al.**⁽¹⁹⁾ and **Ahmed NU et al**⁽²³⁾ study was also found similar findings for Group C and Group F. **Kumar R. et al**⁽¹⁷⁾ study also found similar findings for Group F and Group N.

Side Effect And Complications

In our present study we observed no significant side effect related to study drugs in any of the three groups. No significant bradycardia, hypotension, shivering, sedation was seen in any of the three groups. In accordance with our study **Kumar R et al**⁽¹⁷⁾ also observed no significant side effect in group F and group N, similarly studies conducted by **Puri et al**⁽²⁰⁾ and **Naveen P et al**⁽¹⁹⁾ also found no significant side effect in the study groups.

CONCLUSION

Clonidine when used as an adjuvant causes early onset of both sensory and motor block in brachial plexus block and also prolongs the duration of motor block as compared to other two groups, whereas duration of sensory block was most prolonged in Nalbuphine group as compared to other two groups. No study drug showed any significant side effect.

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