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COMPARATIVE STUDY BETWEEN CLONIDINE AND DEXMEDETOMIDINE AS AN ADJUVANT TO ROPIVACAINE IN SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

Dr. Major T.V. Sreekrishna	Assistant Professor, Dept. of Anaesthesiology, Andhra Medical College, Visakhapatnam, AP.
Dr. Kadiri Srujana	Senior Resident, Dept. of Anaesthesiology, Andhra Medical College, Visakhapatnam, AP.
Dr K. Aparanji	Associate Professor, Dept. of Anaesthesiology, Andhra Medical College, Visakhapatnam, AP.
Dr. Vommi Venkata Ramesh*	Assistant Professor, Dept. of Anaesthesiology, Andhra Medical College, Visakhapatnam, AP. *Corresponding Author

ABSTRACT

BACKGROUND: Upper limb surgeries are widely performed under regional anesthesia with brachial plexus block to provide anesthesia and postoperative analgesia. Bupivacaine is the widely used local anesthetic, but ropivacaine is being used successfully as it is less cardiotoxic, less arrhythmogenic. The addition of adjuvants to local anesthetics enhances the quality and duration of analgesia.

AIM: To compare the effectiveness of clonidine and dexmedetomidine as adjuvants to ropivacaine in supraclavicular brachial plexus block.

MATERIALS & METHOD: Sixty patients of ASA I and II undergoing elective upper limb surgeries under supraclavicular brachial block were randomly divided into two groups(30 each). GROUP D patients received 30ml of 0.5% ropivacaine with 20 µg dexmedetomidine and GROUP C received 30ml of 0.5% ropivacaine with 50µg clonidine. Time of onset and duration of sensory and motor block, duration of analgesia were compared.

RESULTS: Demographic parameters were comparable between the two groups. The onset of sensory block in group C is 9.46 ± 1.50 min, and group D is7.56 ± 1.81 min(<0.0019). The onset of motor block in group C is 13.6 ± 2.23 min and group D is 11.7 ± 2.28 min(<0.0001). Duration of sensory in group C and group D is 532.3 ± 46.82 min and 683.83 ± 96.96 min respectively(<0.0001). Duration of motor block in group C and group D is 475.5 ± 38.80 min and 618.7 ± 100.7 min respectively(<0.0001). Duration of analgesia in group C is 581.83 ± 39.02 min and group D is770.66 ± 110.19 min(<0.0001). Significant difference observed in duration of sensory, motor block, and analgesia between the two groups.

CONCLUSION: Dexmedetomidine is a better adjuvant to ropivacaine than clonidine as it enhances the duration of block and analgesia without adverse hemodynamic consequences.

KEYWORDS : Dexmeditomidine, clonidine,Supraclavicular brachial plexus block, bupivacaine.

INTRODUCTION:

Peripheral nerve blocks have a prominent role in modern anesthesia as they provide ideal operative conditions and excellent postoperative analgesia without any systemic side effects[1]. Brachial plexus block is an alternative to general anesthesia for upper limb surgeries. It is the popular choice of anesthesia for upper limb surgeries as it minimally alters the systemic physiology, a better option for daycare and emergency surgeries, and in critically ill patients where general anesthesia is undesirable[2]. The use of ultrasound guidance increases the accuracy and safety of the block.

Bupivacaine, an amide group local anesthetic, is in use because of its high potency and prolonged duration of action. One of the disadvantages is that it is cardiotoxic with inadvertent injection into the artery. Ropivacaine is an amide local anesthetic prepared as S enantiomer, and it is less cardiotoxic, less arrhythmogenic, and less toxic to the central nervous system than bupivacaine, and it also has intrinsic vasoconstrictor property[3]. The major limitation of regional anesthesia is short duration of action and limited period of postoperative analgesia. So various adjuvants, i.e., Opioids, Midazolam, Neostigmine, Ketamine, have been tried to overcome these limitations and potentiate the efficacy of block[4]. Demirel et al.[5] studied intrathecal midazolam and neostigmine in an animal model and found it to be neurotoxic. The use of ketamine in peripheral nerve blocks has shown to be associated with psychomimetic sequelae without any increase in block duration[6].

Due to these conflicting results, studies continued in search of the ideal adjuvant, which could provide further improvements in operative conditions without side effects.

Presently, alpha-2 agonists have been in focus for their sedative, analgesic, intraoperative, & postoperative hemodynamic stabilizing effects with reduced anesthetic requirements. Clonidine is an alpha-2 adrenergic agonist with few alpha-1 agonist properties and is used to prolong the duration of analgesia as an adjuvant to local anesthetic agents[7].

Dexmedetomidine, potent α2 agonist, is nearly eight times more selective to α2 receptors than clonidine[8]. Dexmedetomidine increases the duration of block and postoperative analgesia when used along with local anesthetics in various regional nerve blocks[9]. Abdallah et al[10] examined various doses of dexmedetomidine (30µg, 100µg, 0.75µg/kg, 1µg/kg) as an adjunct for brachial plexus block and found that dexmedetomidine significantly prolonged the block, but observed reversible bradycardia as an adverse effect which may be due to high dose of dexmedetomidine used.

Hence, the current study was planned with minimizing the dose of dexmedetomidine(20µg) and to compare the efficacy of clonidine (50µg) and dexmedetomidine(20µg) as additives to 0.5% ropivacaine in supraclavicular brachial plexus block.

AIMS AND OBJECTIVES OF THE STUDY :

To evaluate and compare the anesthetic and analgesic effect of clonidine and dexmedetomidine as adjuncts to ropivacaine in supraclavicular brachial plexus block with respect to time of onset of block and duration of sensory and motor block, duration of postoperative analgesia and complications, if any.

PATIENTS AND METHODS:

The present study was conducted at the Department of Anesthesiology, King George Hospital, Visakhapatnam, after obtaining approval from the Institutional Scientific and Ethics Committee. Written and informed consent taken from all patients who participated in the study. This study is a randomized, comparative study. Sixty patients of American Society of Anesthesiologists (ASA) I and II physical status between the age group 18 and 60 years scheduled to undergo elective upper limb surgery were randomly assigned to two groups C and D (n = 30 patients/group)

Group C: 30ml of Ropivacaine 0.5% + Clonidine (50µg)

Group D: 30ml of Ropivacaine 0.5% + Dexmedetomidine(20µg)

Inclusion Criteria:
ASA I and II physical status, age between 18 to 60 years of both genders undergoing upper limb surgeries.

Exclusion Criteria:
ASA III and above, patients without valid informed consent, patients with coagulopathy or using anticoagulants, patients with central and peripheral neuropathy, local cutaneous infections, pregnant and lactating patients, patients with known hypersensitivity to study drugs, patients with severe cardiopulmonary disorders, patients with pneumothorax and chest injuries, patients with personality disorders, partial or unsuccessful block.

Preoperative procedure:
Preanesthetic evaluation was done before surgery and patients who fulfilled the requirement selected for the study. The patient was informed about the anesthesia procedure, drugs used, its effects, and side effects. Written and informed consent taken. Visual analogue scale explained to the patient. Patients randomly divided into two groups C and D, of thirty each. All patients were premedicated with tab alprazolam 0.5 mg the night before the surgery.

Intraoperative procedure:
Intravenous access secured with 18G cannula on non-operated hand, and infusion with Ringer Lactate started. All patients were given Inj Ondansetron 4 mg iv 15 mins before the procedure. All the emergency equipment and drugs needed for the administration of general anesthesia and resuscitation were kept ready. Patients were connected to noninvasive monitors like pulse oximetry, noninvasive blood pressure monitor, and five lead ECG. Baseline parameters recorded, i.e., pulse rate, systolic, and diastolic blood pressure, SPO2. Strict aseptic conditions observed while performing the procedure as for any surgical procedure**.** The patient placed in supine position with the head turned to the opposite side and arm adducted. Under strict aseptic conditions, supraclavicular brachial plexus block was performed with USG guidance (SonoSite) by in plane technique using 6-13 Hz probe and the study drug was injected.

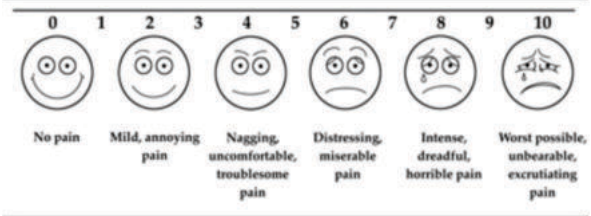
An assessment was made for the following parameters:
1. Onset and duration of Sensory block: Sensory block assessed by pinprick test using the blunt end of a 26-gauge needle at each minute after completion of drug injection in the dermatomal areas corresponding to the median, ulnar, radial, and musculocutaneous nerves till complete blockade. Sensory block assessed by a 3-point scale: 0 - normal sensation, 1 - Loss of sensation of pinprick (analgesia), 2 - Loss of sensation of touch (anesthesia).

Onset time – It is defined as the time interval between the end of total local anesthetic drug administration and complete sensory block (score 2). **Duration of the sensory block** – It is defined as the time interval between the onset of block and resolution of anesthesia (score 0).

2.Onset and duration of motor block: Motor blockade assessed by Modified Bromage Scale: 0 - Normal motor function, 1- Ability to move only fingers, 2- Complete motor block with an inability to move elbow, wrist, and finger.

Motor block onset time - defined as the time interval between the end of total local anesthetic administration and complete motor block (MBS score 2). **Duration of motor block** - defined as the time interval from the onset to the recovery of complete motor function (MBS score 0).

3.Duration of analgesia or first request for analgesia: The pain was assessed using a standard 10 cm Visual Analogue Scale (VAS). Time for the first request for postoperative analgesia (duration of analgesia) was noted. Intravenous inj. Tramadol 100mg with inj. Ondansetron 4mg was given as a rescue analgesic if the VAS score was more than or equal to 4.



HEMODYNAMIC PARAMETERS:
During the intraoperative period, patients were monitored for hemodynamic variables like heart rate, systolic, diastolic, and mean arterial pressures every 5 minutes during the first 15mins, then every 15 mins throughout the surgery and hourly thereafter. Each patient was observed for complications such as bradycardia (heart rate <50 bpm), hypotension(drop in systolic BP >20% of baseline), respiratory depression- (RR<8/min or SPO2 <90%), pneumothorax, horner's syndrome, hematoma at the site of injection, nausea, vomiting.

STATISTICALANALYSIS:
Data entered in Microsoft MS Excel sheet and analysis was done using GRAPHPAD software on personal computer. Continous data such as onset, duration expressed as mean and standard deviation and analyzed using student t-test. Categorical data expressed as proportions and analyzed using the chi-square test. A p-value of < 0.05 is considered to be statistically significant.

RESULTS:
There was no statistically significant difference observed between the two groups with respect to age, weight, sex ratio with p value >0.05 (Table 1). The mean onset time of sensory block in group C is 9.46 ± 1.50 min and group D is 7.56±1.81 min. The mean onset time of motor block in group C is13.6 ± 2.23 min and group D is 11.7±2.28 min (Table 2). Statistically significant difference present between the two groups as p value is <0.05 and onset of the sensory and motor block was faster in group D than group C. Mean duration of sensory block in group C is 532.3 ± 46.82 min and group D is 683.83±96.96 min. Mean duration of motor block in group C is 475.5 ± 38.80 min and group D is 618.7±100.7 min (Table-2). Significantly longer duration of sensory and motor block was observed in Group D than Group C (p<0.0001). Significant increase in mean duration of analgesia in group D was noted (770.66±110.19 min) as compared to group C (581.83 ± 39.02 min) and the difference is statistically significant (p value<0.0001).

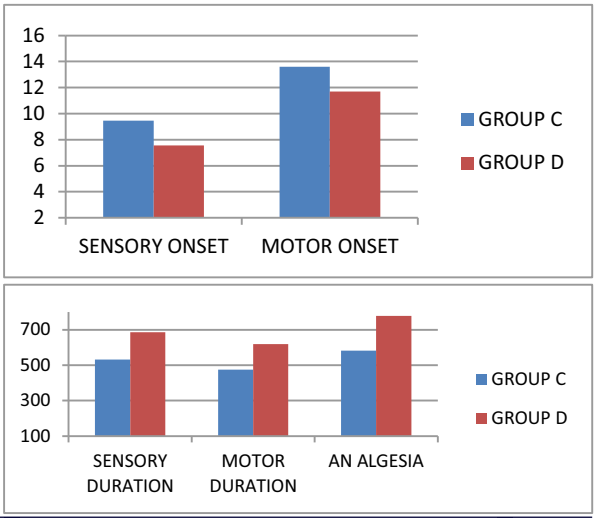
Table 1: Demographic characteristics

Demographic profile	Group C	Group D	P value	
Sex (m:f)	18:12	19:11	1.0	Not significant
Mean age(yr)	39.7±13.3	37.3±14.7	0.50	Not significant
Mean weight(kg)	57.7 ± 8.02	58.4 ± 8.2	0.73	Not significant

Table 2: Onset of sensory and motor block

	GROUP C	GROUP D	P VALUE
ONSET OF SENSORY BLOCK	9.46 ± 1.50 min	7.56 ± 1.81min	<0.0001 (SIGNIFICANT)
ONSET OF MOTOR BLOCK	13.6 ± 2.23 min	11.7 ± 2.2 min	<0.0016 (SIGNIFICANT)
SENSORY BLOCK DURATION	532.3 ± 46.82 min	685 ± 97.8min	<0.0001 (SIGNIFICANT)
MOTOR BLOCK DURATION	475.5 ± 38.80 min	618.7± 100.7 min	<0.0001 (SIGNIFICANT)
DURATION OF ANALGESIA	581.83 ± 39.02 min	777.8± 116.6 min	<0.0001 (SIGNIFICANT)

Figure1: Onset and duration of sensory and motor block



DISCUSSION:

Brachial plexus block provides both anesthesia and postoperative analgesia for upper limb procedures. It has an advantage over general anesthesia like avoiding airway instrumentation, decreased incidence of nausea and vomiting, early mobilization, and extended postoperative analgesia[11]. Of various approaches to brachial plexus, the supraclavicular route is preferred as there will be rapid, dense, and predictable anesthesia and analgesia of the entire limb.

The accuracy of the block is increased with the use of ultrasound guidance, and the problems associated with the conventional technique like patient discomfort to paresthesia, injury to the nerve and surrounding structures avoided.

Many systemic reviews of various adjuvants for brachial plexus blocks indicate that alpha - 2 agonists have excellent analgesic benefits with minimal adverse effects [12].

The α2 agonists enhance local anesthetic potency and prolong its duration in a dose-dependent manner by combining with the α2 receptors at the peripheral level. The possible mechanisms by which the α2 agonists improve local anesthetic action include vasoconstriction around the site of injection, thus delaying the absorption of local anesthetic drugs, resulting in a prolongation of the effect. Other mechanisms include the release of local enkephalins like substances, a decrease in the release of local inflammatory mediators, and an increase in the release of anti- inflammatory cytokines.

Both groups were standardized with respect to the volume of drug injected and supraclavicular block performed using the USG technique. Continuous hemodynamic monitoring was done throughout the procedure. The demographic variables like age, weight, sex, ASA grade were similar between the two groups. The statistical analysis of demographic variables was done using the standard error of the difference between the means and chi-square test. The p-value is >0.05, suggesting statistically insignificant.

In this study, statistically significant difference (p-value <0.05) is observed in the mean onset time of sensory and motor block between the two groups and it implies that the onset time of sensory and motor block in group D is faster than in group C. The more lipid solubility and greater affinity of dexmedetomidine to α2 adrenergic receptors than clonidine might have led to quicker of onset of block.

In our present study, statistically significant difference (p-value<0.05) is present between the two groups with respect to duration of block suggesting that the duration of the sensory and motor block significantly prolonged in group D when compared with group C. The probable mechanism of increased duration of block is due to enhancement of the hyperpolarisation which prevents the nerve from returning to resting membrane potential for subsequent firing[13].

The proposed mechanisms for the significant decrease in analgesic consumption in the postoperative period with the use of adjuvants like dexmedetomidine and clonidine are centrally mediated analgesia, α2 β adrenoceptor-mediated vasoconstrictive effects, attenuation of an inflammatory response and direct action on peripheral nerve[14]. The prolongation of analgesia after neural blockade with the use of α agonists is due to an increase in potassium conductance and blocking the conduction of C and A fibers[15].

The direct action of α2-adrenoceptor agonists on the nerve can be explained based on a study conducted by **Dalle *et al***.[16] They proved that α2- agonist inhibits the hyperpolarization-activated cation (Ih) current. The Ih current plays a key role in cell excitability, in both the central and peripheral nervous systems and normally acts to reset a nerve for subsequent action potentials. Therefore, by blocking the Ih current, α2-adrenoceptor agonist enhances hyperpolarization and inhibits subsequent action potentials.

Don Sebastian et al.[17] compared clonidine(1μg/kg) and dexmedetomidine (1μg/kg) as an adjunct to 0.5% ropivacaine, and observed a faster onset time and prolongation of block with dexmedetomidine compared to clonidine.

Qazi Ehsan Ali et al.[18] conducted a study to evaluate the effects of clonidine with ropivacaine and observed the mean onset time of sensory block in group C is 9.1±3.16 mins. These results were comparable to our study. Studies conducted by **Brajesh yadav**[19] and **Usha Bafna et al**.[20] comparing clonidine and dexmedetomidine, observed a statistically significant difference between groups and concluded that mean onset time of motor block is earlier in group D than group C.

J.Chinnappa et al.[21] conducted a study to compare dexmedetomidine (1μg/kg) in addition to 30 ml of 0.5% ropivacaine using nerve stimulation technique. They observed that the mean onset time of sensory block was 9.5±5.8 mins, and the mean onset time of motor block was 15.6±6.3 mins. These results were comparable to our present study.

A study was undertaken by **Nazir et al.**[22] to evaluate and compare the effects of clonidine (50μg), and dexmedetomidine(50μg) added to 0.5% ropivacaine and noticed that dexmedetomidine has prolonged the duration of sensory and motor than clonidine. The results of their study were comparable to the present study.

In the present study, the baseline pulse rate in group C was 78.4±4.39, and group D was 78±4.23. There was fall a in pulse rate compared to baseline from 10 minutes to 60 minutes, which continued up to 2 hours in group D, and the lowest pulse rate was 66.03±5.35, and in group C the lowest pulse rate was 70.3±3.88. However, this fall in pulse rate was within the physiological range. None of the patients developed bradycardia (pulse rate below 50). There was a statistically significant difference in pulse rate between two groups intraoperatively, but it not clinically significant.

Presynaptic activation of α2 adrenoceptor in the central nervous system inhibits the release of norepinephrine and terminates the propagation of pain signals whereas their postsynaptic activation inhibits sympathetic activity, thereby decreasing HR and BP[23].

The baseline systolic blood pressure in group C was 118.86 ± 6.35, and in group D was 119.83 ± 7.20. There was no statistically significant decrease in mean systolic blood pressure between the two groups. The lowest systolic blood pressure in group C was 109.2 ± 6.06 mmHg and in group D lowest blood pressure 111 ± 6.35 mmHg. However, this fall in systolic blood pressure was within physiological range. The baseline diastolic blood pressure in group C was 74.76 ± 7.10mmHg and in group D was 72.6±4.33 mmHg. There was no statistically significant difference in mean diastolic blood pressure between the two groups.

In the study done by **Esmaogolu et al**.[9] there was a significant fall in heart rate, systolic, and diastolic blood pressure which is due to larger doses of dexmedetomidine(100 micro gms) used in their study. In the present study, there was no significant difference observed in hemodynamic parameters which might be due to the low of dexmedetomidine (20μg) used.

In our study, no patient developed any severe complications due to block procedure. The heart rate, blood pressure, and saturation are within physiological limits and the patient is hemodynamically stable with not much variability.

The use of USG in brachial plexus block requires considerable training and knowledge of the equipment and cross-sectional regional nerve block anatomy.

The limitation of this study is that quality of block and plasma levels of the drug were not assessed.

The present study is limited to fixed concentration and dose of ropivacaine added to adjuvants. In future, as the use of ultrasound imaging provides accurate nerve localization and visualization of local anesthetic spread, the effect of a reduced volume and concentration of local anesthetic can be studied.

CONCLUSION:

The addition of dexmedetomidine (20μg) to 0.5 % ropivacaine in usg supraclavicular brachial plexus block had faster onset, greater duration of sensory and motor block, and also, increased the duration of analgesia when compared to clonidine (50μg) without significant hemodynamic alterations. Dexmedetomidine is better adjuvant than clonidine when added to ropivacaine in supraclavicular brachial plexus block.

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