Original Article

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Efficacy of Clonidine versus Dexmedetomidine as Adjuvants to 0.5% Ropivacaine in Nerve Stimulator Guided Supraclavicular Brachial Plexus Block- A Randomised Clinical Study

Anaesthesia Section

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ABSTRACT

Introduction: Supraclavicular brachial plexus block is used for providing pain relief in upper limb surgeries and has many advantages over general anaesthesia. Alpha-2-adrenergic agonists are chosen with local anaesthetics for their sedative, analgesic and antihypertensive properties.

Aim: To compare the efficacy of clonidine and dexmedetomidine when added to 0.5% ropivacaine in nerve stimulator guided supraclavicular block when performed for upper limb surgeries.

Materials and Methods: This randomised clinical study was conducted in the Department of Anaesthesia Mata Chanan Devi Hospital, New Delhi, India (tertiary care center), from September 2015 to September 2016. Total 90 patients were randomly allocated into three groups. Group A {Inj. ropivacaine 0.5% (29 mL)+ normal saline 1 mL to make 30 mL}, group B {Inj. ropivacaine 0.5% (29 mL)+ clonidine 1 µg kg-1 to make 30 mL) and group C {Inj. ropivacaine 0.5% (29 mL)+ dexmedetomidine 1 µg kg-1 to make 30 mL}. Parameters observed included onset of sensory and motor block, total motor duration, postoperative analgesia as primary outcome; and intraoperative haemodynamic parameters and side effects as secondary outcome.

Results: All the three groups were found to be similar with demographic profile. Patients in dexmedetomidine group showed faster onset and longer duration of sensory and motor blocks (p-value<0.01). The mean onset of sensory block in minutes was 12.03±2.20, 8.20±1.40, 6.80±1.35 in groups A, B and C, respectively (p-value<0.001). The mean onset of motor block in minutes was 18.47±2.78, 13.37±2.86 and 11.30±2.04 in group A, group B and C, respectively (p-value<0.001). The mean duration of analgesia in group A, B and C was 555.17±65.36, 710.00±73.58 and 902.67±116.65 minutes, respectively (p-value<0.001). The mean duration of motor block in group A, group B and group C were 330.00±51.78, 418.17±38.29 and 516.83±50.33 minutes, respectively (p<0.0001). The duration of postoperative analgesia and total motor duration were significantly prolonged in dexmedetomidine group than group A and B.

Conclusion: It can be concluded that both clonidine and dexmedetomidine increases the total motor duration and postoperative analgesia when added to ropivacaine, but dexmedetomidine is a better choice when used in supraclavicular block, without any significant side-effects.

Keywords: Local anaesthetic, Peripheral nerve block, Postoperative pain, Pain score, Total motor duration

INTRODUCTION

From the operative suite, the role of peripheral nerve blockade was expanded for management of postoperative pain and chronic pain. In particular, managing pain after orthopaedic procedures poses a challenge to both anaesthesiologists and orthopaedic surgeons. In an effort to improve analgesia and facilitate mobilisation, brachial plexus block is often used as primary anaesthetic or can also be used along with general anaesthesia for pain relief in orthopaedic procedures. This can avoid multiple drugs used in general anaesthesia and decreases postoperative nausea and vomiting [1]. The most common local anaesthetic used is bupivacaine. Ropivacaine is less lipophilic than bupivacaine and that together with its stereo selective properties contributes to ropivacaine having a higher threshold for cardiovascular and central nervous system toxicity [2]. Increasing the duration of local anaesthetic action is often desirable because it prolongs surgical anaesthesia and analgesia. Vasoconstrictors can be used to vasoconstrict vessels, thereby reducing vascular absorption of the local anaesthetic. Additives like opioids, steroids, verapamil were added to local anaesthetics, but associated with side-effects.

Alpha-2-adrenergic agonists became popular recently because of their sedative, analgesic and antihypertensive actions. Clonidine, alpha-2 agonist when combined with local anaesthetic has been found to extend the duration of nerve blocks [3]. Dexmedetomidine, a highly selective alpha-2 agonist, with an affinity eight times greater than clonidine has better analgesic properties in peripheral nerve blocks [4-7].

Till now most studies have used dexmedetomidine and clonidine with bupivacaine. This clinical trial compared dexmedetomidine with clonidine with respect to duration of block and postoperative analgesia as an adjuvant to ropivacaine. This randomised clinical study was conducted to compare the efficacy of alpha-2 agonists clonidine and dexmedetomidine when added to 0.5% ropivacaine in nerve stimulator guided supraclavicular block when performed for upper limb surgeries. Parameters observed included onset of sensory and motor block, total motor duration, postoperative analgesia as primary outcome measures; and intraoperative haemodynamic parameters and side-effects as secondary outcome measures.

MATERIALS AND METHODS

This randomised clinical study was conducted in the Department of Anaesthesia Mata Chanan Devi Hospital, New Delhi, India (tertiary care center), from September 2015 to September 2016. The ethical clearance was obtained from the Institutional Ethics Review Committee (no.9-141/DNB/2015-16/MCDH-2506) and preoperatively, informed written consent of the patient was taken for participation in the study.

Inclusion and Exclusion criteria: The study included Patients with American Society of Anaesthesiologists' (ASA) grade I, II and aged between 18 to 60 years of either sex, presenting for upper limb surgery were included in the study. Patients with severe cardiac, renal or hepatic disorders and those allergic to local anaesthetic agents were excluded from the study.

Sample Size: An important parameter is the duration of analgesia which was recorded as 488±65.04 mins for Ropivacaine (Usha Bafna et al.,) [10], 654±90 mins for Ropivacaine+Dexmed (Nasir Uddin Admed et al.,) and 720.83±44.16 mins for Ropivacaine+Dexmed (Don Sebastian et al.,) [11] Assuming these as reference values, the minimum required sample size at 5% level of significance and 95% power was obtained for various combination of groups.

Formula used:

$$n = \frac{2}{d^2} C_{p,\ power}$$

where

n is the number of subject required in each group

d is the standardized difference and

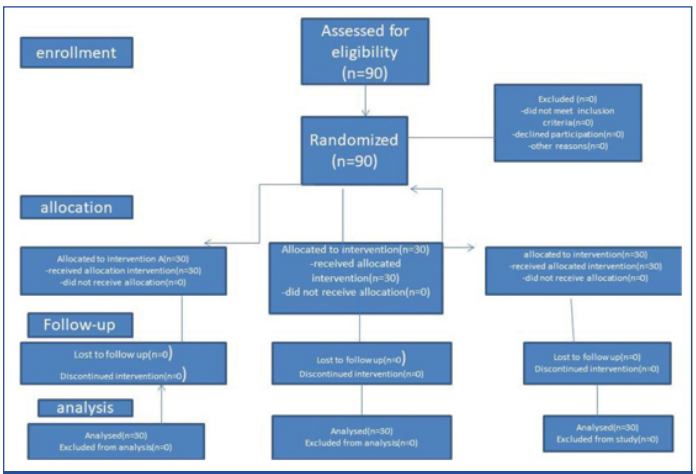
$C_{p,\ power}$ is the constant defined by the values chosen for the p-value and power

Calculations:

$$d = \frac{(720.83 - 654)}{\sqrt{\frac{90^2 + 44.16^2}{2}}} = 0.9428$$

$C_{5\%,\ 95\%}$ =13 (from tables)

The allocation of patients to the three groups was random and done through a computer generated sequence of random alphabets C and D denoting (Ropivacaine+Clonidine) and (Ropivacaine+Dexmed) respectively. The Microsoft Excel command used to generate this random sequence was "=if (rand()<0.5,"C","D")" which was copied and pasted to cells to obtain the sequence [Table/Fig-1]:



[Table/Fig-1]: Consolidated Standards of Reporting Trials (CONSORT) flow chart.

Group A (n=30): Inj. ropivacaine 0.5% (29 mL)+ normal saline 1 mL to make 30 mL.

Group B (n=30): Inj. ropivacaine 0.5% (29 mL)+ clonidine 1 µg kg-1 to make 30 mL.

Group C (n=30): Inj. ropivacaine 0.5% (29 mL)+ dexmedetomidine 1 µg kg^{-1} to make 30 mL.

Study Procedure

In each patient, thorough history was elicited. All patients were kept 6 hours of fasting prior to surgery. Tablet alprazolam (0.25 mg) was used as a premedication to be given on night before surgery. After arrival of patients in the operating table, standard monitors were attached-pulse oximetry (SpO_2), Cardio scope for rate and rhythm, non invasive blood pressure monitoring. A 18 G cannula was secured in all patients in operating room and an intravenous drip was started. Sedation was given using intravenous midazolam 0.02 mg/kg. The procedure was thoroughly explained to the patient and consent of the patient was taken. Supraclavicular block was performed with the help of nerve stimulator technique. Identical syringes were prepared by the anaesthesiologist not involved with the conduct of the study. The patient was placed in the supine position and head turned to the opposite side to the one being blocked. The patient was asked to lower the shoulder and flex the elbow, in order that the forearm rests on his/her lap. The interscalene groove was palpated posterior to the subclavian artery pulse just medial to the midpoint of the clavicle. After a skin wheal, a 22-gauge, 1.5 inch needle was directed just above and posterior to the subclavian pulse and was advanced until a paraesthesia is encountered or muscle contraction is noted. The point of needle entrance was about 1 inch (2.5 cm) lateral to the insertion of the sternocleidomastoid muscle in the clavicle. Palpation of the subclavian artery at this site confirms the landmark. The palpating index finger was placed at this site. The needle was connected to a nerve locator by the electrodes and was properly grounded with the help of Electrocardiogram (ECG) lead. Stimulation was started with an intensity of 2.0 mA and a pulse width of 100 µs. If contraction is still observed or palpated with the stimulator voltage decreased to 0.5 mA, then 30 mL of local anaesthetic is injected. The site of injection was sealed with tincture benzoin. The patient was observed for any complications of the block at 5 minutes interval time for 30 minutes duration.

Following measures were recorded during the study:

1. **Time of sensory onset:** Sensory block was assessed by cold alcohol swab along the operative field proximally and distally as well.
2. **Time of motor onset:** Motor block was determined according to modified bromage scale for upper extremities on a 3-point scale.
3. **Total motor duration:** Motor block was evaluated and recorded at an interval of every 30 minutes till the time when bromage scale was <3 in the postoperative period.
4. **Timing till first analgesic requirement:** During the procedure, anaesthesia was considered satisfactory if the patient did not complain of any pain or discomfort.

Postoperatively patient was followed-up in the recovery and postoperative ward. Pain was assessed using the 0-10 Visual Analogue Score (VAS) at interval of half an hour for first 8 hours and then hourly till 24 hours. When the VAS >4, rescue analgesic (intravenous diclofenac 1 to 1.5 mg/kg) was given.

5. **Haemodynamic variables:** Patients heart rate, mean blood pressure and oxygen saturation were monitored every 15 minutes in first hour then every 30 minutes for further 2 hours. And then every 2 hours till the need of rescue analgesia.
6. **Side-effects** (if present): Incidence of drowsiness, pruritus, nausea/vomiting, hypotension, bradycardia, Horner's syndrome, phrenic nerve palsy, pneumothorax, respiratory depression and sign and symptoms for local anaesthetic toxicity were looked for and noted, if any.

STATISTICAL ANALYSIS

The quantitative variables in both groups were expressed as mean±SD and compared using Analysis of Variance (ANOVA) and Unpaired t-test between groups and Paired t-test within each group at various follow-ups. The qualitative variables were expressed as frequencies/percentages and compared using Chi-square test. A p-value<0.05 was considered statistically significant. Statistical Package for Social sciences (SPSS) version 15.0 was used for statistical analysis.

RESULTS

All the three groups had comparable demographic profile and also the duration of surgery [Table/Fig-2].

Demographic data	Group A	Group B	Group C	p-value
Age (years)	42.30±14.53	36.60±16.13	42.07±14.60	0.26
Height (cm)	164.97±5.81	165.23±5.85	164.03±5.33	0.691
Weight (kg)	66.67±7.92	66.47±7.68	64.87±7.30	0.608
Duration of surgery (min)	116.50±59.16	116.20±57.70	132.40±82.63	0.57

[Table/Fig-2]: Demographic profile.

Onset of sensory blockade was faster in group C than with clonidine and plain ropivacaine.Onset of motor blockade was faster in group C than with clonidine and plain ropivacaine. There was a significant prolongation of duration of analgesia in group C than group B and A. There was significant prolongation of duration of motor block in group C than group A and B [Table/Fig-3]. There was a significant lowering of heart rate and mean blood pressure in group B and C at 45, 60, 90 and 120 minutes compared to group A. Heart rate and mean blood pressure were comparable between clonidine and dexmedetomidine group. There was no significant difference in SpO_2 levels between the groups during the surgery and in the postoperative period [Table/Fig-4,5].

Parameters	(Mean±SD)	p-value
Onset of sensory block (minutes)		
Group A	12.03±2.20	<0.001 A vs B
Group B	8.20±1.40	0.005 B vs C
Group C	6.80±1.35	<0.001 A vs C
Onset of motor block (minutes)		
Group A	18.47±2.78	<0.001 A vs B
Group B	13.37±1.71	0.001 B vs C
Group C	11.30±2.04	<0.001 A vs C
Total analgesic duration (minutes)		
Group A	555.17±65.36	<0.001 A vs B
Group B	710.00±73.58	<0.001B vs C
Group C	902.67±116.65	<0.001 A vs C
Duration of motor block (minutes)		
Group A	330.00±51.78	0.013 A vs B
Group B	418.17±38.29	<0.001 B vs C
Group C	516.83±50.33	<0.001 A vs C

[Table/Fig-3]: Onset of sensory blockade, motor block, duration of analegesia and duration of motor block in three groups.
p-value<0.05 was considered as statistically significant

Dependent variable Heart rate	(I) Group	(J) Group	Mean difference (I-J)	p-value
At 0 min	Group A	Group B	-0.13333	0.997
		Group C	-0.13333	0.997
	Group B	Group C	0	1
At15 min	Group A	Group B	-0.13333	0.997
		Group C	2.4	0.375
	Group B	Group C	2.53333	0.336
At 30 min	Group A	Group B	0.86667	0.872
		Group C	5.16667*	0.011
	Group B	Group C	4.30000*	0.04
At 45 min	Group A	Group B	1.73333	0.558
		Group C	5.03333*	0.01
	Group B	Group C	3.3	0.127
At 60 min	Group A	Group B	2.13333	0.385
		Group C	5.00000*	0.007
	Group B	Group C	2.86667	0.182
At 120 min	Group A	Group B	2.83333	0.163
		Group C	5.03333*	0.004
	Group B	Group C	2.2	0.331
At 180 min	Group A	Group B	4.63333*	0.007
		Group C	5.43333*	0.001
	Group B	Group C	0.8	0.853

[Table/Fig-4]: Heart rate among three groups at various time intervals.

Dependent variable Mean arterial pressure	(I) Group	(J) Group	Mean Difference (I-J)	p-value
At 0 min	Group A	Group B	1.66667	0.57
		Group C	2.13333	0.40
	Group B	Group C	0.46667	0.96
At 15 min	Group A	Group B	2.53333	0.27
		Group C	2.9	0.18
	Group B	Group C	0.36667	0.97
At 30 min	Group A	Group B	2.86667	0.17
		Group C	3.43333	0.08
	Group B	Group C	0.56667	0.93
At 45 min	Group A	Group B	3.90000*	0.05
		Group C	4.43333*	0.02
	Group B	Group C	0.53333	0.94
At 60 min	Group A	Group B	4.26667*	0.02
		Group C	4.50000*	0.01
	Group B	Group C	0.23333	0.99
At 120 min	Group A	Group B	4.76667*	0.01
		Group C	4.13333*	0.03
	Group B	Group C	-0.63333	0.91
At 180 min	Group A	Group B	7.13333*	<0.001
		Group C	5.50000*	<0.001
	Group B	Group C	-1.63333	0.53

[Table/Fig-5]: Mean blood pressure at various time interval.
*The mean difference is significant at the 0.05 level

DISCUSSION

Supraclavicular brachial plexus block is used as a regional nerve block to provide anaesthesia and analgesia for the upper limb surgery. It is the most effective block for all the portions of the upper limb and is carried out at the "division" level of the brachial plexus [7]. Ropivacaine and bupivacaine alone provided better operating conditions but the duration of analgesia is not maintained for prolonged period. Addition of alpha 2 adrenoceptors [9] clonidine and dexmedetomidine, to ropivacaine effectively and significantly prolongs the duration of analgesia as well as produces earlier onset of actionnerve stimulator technique is better than the conventional landmark technique [8]. Ropivacaine is cardiostable than bupivacaine and is thus used in the present study [6].

Parameters observed in the present study were postoperative analgesia as primary outcome and onset, duration of sensory and motor block, haemodynamic variables as secondary outcomes. The mean onset of sensory block and motor block in minutes was found to be faster in group C than group A and B. Sensory and motor onset duration was faster in dexmedetomidine group than the other two groups.

Bafna U et al., compared the effect of dexmedetomidine and clonidine in supraclavicular brachial plexus block. They also found a

significant difference in the onset of sensory and motor block time. It was faster in dexmedetomidine group than clonidine and plain ropivacaine group [10].

Don Sebastian et al., also compared the effect of clonidine and dexmedetomidine with ropivacaine and found a faster onset time of sensory and motor block in dexmedetomidine group than clonidine group [11]. Esmaoglu A et al., and Aggarwal S et al., have also concluded that dexmedetomidine when added to local anaesthetic agents prolonged the duration of motor block. It also resulted in faster onset of sensory and motor block [6,13]. In the present study, the duration of postoperative analgesia and total motor duration were significantly prolonged in dexmedetomidine group than with clonidine and plain ropivacaine. Similarly, a few other studies have also concluded that dexmedetomidine is a better agent than clonidine and produces prolonged motor block and postoperative analgesia [14-16]. Sebastian D et al., also compared the effects of clonidine and dexmedetomidine and observed that dexmedetomidine is a better agent than clonidine in terms of increased postoperative analgesia in supraclavicular block [11]. Kanvee V et al., and Patki YS et al., also had similar results for their studies [16,17].

The total duration of motor block and postoperative analgesia was significantly prolonged in dexmedetomidine group than in clonidine group. Waindeskar V et al., concluded that dexmedetomidine significantly shortens the onset time and prolongs the duration of sensory and motor blocks and also postoperative analgesia when added to levobupivacaine in ultrasound guided block [18]. The present study reported a significant lowering of heart rate and mean bloodpressure in dexmedetomidine and clonidine group at 45, 60, 90 and 120 minutes compared to plain ropivacaine group. Heart rate and mean blood pressure were comparable between clonidine and dexmedetomidine group. These results are comparable with other studies. Harshavardhana HS, found that pulse rate and mean blood pressure were comparable in dexmedetomidine and clonidine group [13]. Significantly lower pulse rate were observed at 45, 60, 90 and 120 minutes, but not less than 60 beats/min. Similar results were reported by other researchers too [10,11,14]. No patients in the current study had any haemodynamic instability, bradycardia or significant hypotension. No patients developed pneumothorax and horner's syndrome.

Limitations(s)

Ultrasound examination could not be done, and hence the quality of block remained undetermined.

CONCLUSION(S)

Dexmedetomidine, when added to ropivacaine for brachial plexus block using supraclavicular approach, produces prolonged motor block and postoperative analgesia which lasts longer than that produced by ropivacaine alone and with clonidine and without any significant side-effects.

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