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Original Research Paper

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COMPARISON BETWEEN CLONIDINE AND DEXMEDETOMIDINE AS ADJUVANT FOR SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK

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ABSTRACT

Objectives: 1) To compare the efficacy of two alpha2 agonist drugs, namely clonidine and dexmedetomidine when added to levobupivacaine as adjuvant for brachial plexus block for upper limb surgery. We compared the onset and duration of sensory and motor blockade, duration of analgesia, and haemodynamic changes. 2) To study the occurrence of any adverse effect in perioperative period.

Methodology: 140 patients of ASA Class I and II, aged 18-60 years, scheduled for upper limb surgery were studied in a prospective randomized double-blind manner. Supraclavicular brachial plexus block was administered to patients who were randomly divided into two groups – Group A and Group B. For brachial plexus block, Group A received 0.25% levobupivacaine, 0.5ml / Kg, along with clonidine 2mcg/ml. Group B received 0.25% levobupivacaine, 0.5ml / Kg, along with dexmedetomidine 2mcg/ml.

Results: The time of onset of sensory and motor blocks in Group B (dexmedetomidine group) were quicker than that of Group A (clonidine group). Prolongation of sensory and motor blocks and mean duration of analgesia were observed in Group B compared to Group A.

Conclusion: Dexmedetomidine is found to be superior adjuvant than clonidine when used with levobupivacaine for brachial plexus block.

KEYWORDS : Adjuvant, Levobupivacaine, Clonidine, Dexmedetomidine

Introduction:

Brachial plexus block is a popular and widely employed regional nerve block technique for anaesthesia and analgesia for surgery of upper extremity. Local anaesthetic alone for brachial plexus block provides good operating conditions, but has a shorter duration of postoperative analgesia. So various drugs have been used as adjuvants (e.g. dexamethasone, fentanyl, adrenaline, clonidine, dexmedetomidine etc.) with local anaesthetics to hasten the onset of sensory and motor block and to prolong the duration of anaesthesia and analgesia[1]. We compared the efficacy of two alpha2 agonists- Clonidine versus Dexmedetomidine as adjuvant to Levobupivacaine in supraclavicular brachial plexus block in respect to sensory and motor onset, duration of sensory and motor block, duration of analgesia along with haemodynamic variables and side effects profile. It was a prospective, randomized, double-blinded comparative study.

Methodology:

After obtaining permission and informed written consent from the institutional ethical committee of Midnapore Medical College, West Bengal, 140 adult patients aged 18 to 60 years of ASA physical status I and II scheduled for below mid-arm surgery were allocated into two groups –Group A and Group B by computer based randomization table.

Study period: March 2014 to July 2015

Group A: Patients receiving local anaesthetic solution containing 2.5 mg levobupivacaine with clonidine 2mcg per ml in a dose of 0.5 ml/kg.

Group B: Patients receiving local anaesthetic solution containing 2.5 mg levobupivacaine with dexmedetomidine 2 mcg per ml in a dose of 0.5 ml/kg.

Sample size [2] estimation was done after a thorough review of related articles (N-140, n-70) following which an expert clinical guess was performed to derive variables to estimate sample size. Analysis of data was done by SPSS software version 20. Unpaired t-test was applied for demographic data, haemodynamic parameters, onset and duration of sensory and motor blockade and duration of analgesia. P-value was considered significant <0.05 and highly significant if <0.001.

Preoperative instructions:

All patients were instructed not to consume solid food after midnight on the day before surgery but clear fluids were permitted till three hours prior to scheduled time of operation. Tablet ranitidine 150 mg and tablet ranitidine were given at night before surgery.

Monitoring:

After patient's arrival at the operation theatre, multichannel monitor was attached for monitoring of ECG, heart rate, respiratory rate, non-invasive blood pressure (NIBP), peripheral oxygen saturation (SpO2). Baseline heart rate, blood pressure and peripheral oxygen saturation were recorded. Intravenous infusion of Ringers' lactate and oxygen at the rate of 4 litres/minute via face mask were initiated. Patients were administered intravenous midazolam 0.02 mg/kg 15 minutes before brachial plexus block. All local anaesthetic solutions and adjuvant drugs were prepared by an anaesthesiologist who was not involved in the performance of brachial plexus block or data collection. Supraclavicular brachial plexus blocks were performed using nerve stimulator needle.[3]

Occurrences of any complication like bradycardia, hypotension, Horner's syndrome, and clinically significant pneumothorax were noted[4]. The time of occurrence of first postoperative pain and the time of complete recovery of motor functions of the forearm and hand were recorded in every patient. Both patient and observer were also blinded to the group allocation.

Onset of sensory block was assessed by loss of pin prick sensation.
Duration of sensory block is the time interval between loss of pin-prick sensation and appearance of pin prick sensation[6].

Motor block was tested by thumb abduction and wrist extension (radial nerve), thumb adduction and ulnar deviation of the hand (ulnar nerve), flexion of the elbow in supination (musculocutaneous), thumb opposition and wrist flexion (median nerve) and was measured using a Modified Bromage scale for upper extremity[5,6].

Grade 0:- Normal motor function with full flexion and extension of elbow, wrist and fingers.
Grade 1:-Decreased motor strength with ability to move the fingers only.
Grade 2:-Complete motor block with inability to move the fingers.

Onset of motor block is the time interval between the placement of block and appearance of Grade 2 inability in the above scale.

Duration of motor block is the time interval between the onset of block and regain of full motor function as Grade 0.

Duration of analgesia is the time from the onset of sensory block to the requirement of rescue analgesic. Intensity of pain was assessed by visual analogue scale (VAS scale-0-no pain, 10-severe pain) and patient asked for rescue analgesic if he/she felt a pain above 4 in the VAS scale[7].

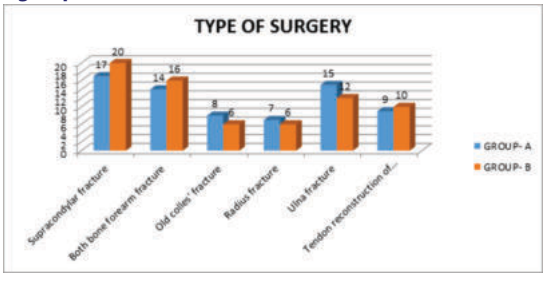
Results:

Table 1: Comparison of Demographic parameters between two study groups

	Group A	Group B	P-value
Age(years)	37.63 ± 12.38	38.03 ± 12.71	0.851
Sex (M: F)	18:17	33:37	0.612
Weight (Kg)	53.35 ± 7.79	53.48 ± 6.59	0.916
Height (cm)	159.74 ± 5.26	159.69 ± 5.66	0.951
ASA I:II	32:3	13:1	0.753

No significant differences were observed on comparing the demographic profiles between the two groups. (P>0.05).

Diagram 1: Comparison of different types of surgery in between two groups



No significant difference was observed between two groups when type of surgery was compared (P>0.05).

Table 2: Duration of surgery in the study groups

	STUDY GROUPS	N	Mean	Std. Deviation	P Value
Duration Of Surgery	GROUP-A	70	67.37	13.50	0.052
	GROUP-B	70	71.77	13.17	

Duration of surgery in Group A and Group B was statistically insignificant.

Table 3: Complete onset of sensory block in the study groups

	STUDY GROUPS	N	Mean	Std. Deviation	P value
Complete onset time of Sensory Block (minutes)	GROUP- A	70	14.31	1.91	<.001
	GROUP- B	70	12.80	1.81	

Mean complete onset time of sensory block was significantly shorter in dexmedetomidine Group (B) than clonidine Group (A).

Table 4: Complete onset of motor block in the study groups

	STUDY GROUPS	N	Mean	Std. Deviation	P value
Complete onset time of Motor Block(minutes)	GROUP- A	70	18.14	2.43	<.001
	GROUP- B	70	16.46	2.21	

Mean complete onset time of motor block was significantly less in dexmedetomidine group than clonidine group.

Table 5: Duration of sensory block in the study groups

	STUDY GROUPS	N	Mean	Std. Deviation	P value
Duration of Sensory Block	GROUP- A	70	474.86	41.16	<.001
	GROUP- B	70	586.71	52.49	

Mean duration of sensory block in Group-B was significantly prolonged than Group A.

Table 6: Duration of motor block in the study groups

	STUDY GROUPS	N	Mean	Std. Deviation	P value
Duration of Motor Block	GROUP- A	70	426.86	33.55	<.001
	GROUP- B	70	531.00	46.34	

Mean duration of motor block in Group-B patients was significantly longer than Group-A.

Table 7: Duration of analgesia in the study groups

	STUDY GROUPS	N	Mean	Std. Deviation	P value
Duration Of Analgesia	GROUP- A	70	539.57	35.19	<.001
	GROUP- B	70	675.00	50.75	

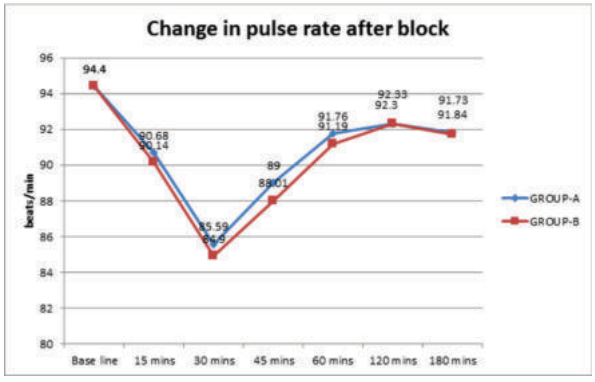
Mean duration of analgesia in Group-B patients was significantly prolonged compared to Group A.

Table 8: Preoperative parameters in the study groups

Pre-operative parameters	STUDY GROUPS	N	Mean	Std. Deviation	P Value
Mean Blood Pressure (mmHg)	GROUP-A	70	94.40	5.76	0.996
	GROUP-B	70	94.40	4.96	
Pulse Rate(beats/min)	GROUP-A	70	77.16	6.57	0.4
	GROUP-B	70	78.06	6.01	
SPO2(%)	GROUP-A	70	98.74	0.81	1.00
	GROUP-B	70	98.74	0.82	

Preoperative mean blood pressure, pulse rate, SPO2 are expressed in mean and standard deviation and no significant difference was observed.

Diagram 2: Change in pulse rate after block in the two study groups:

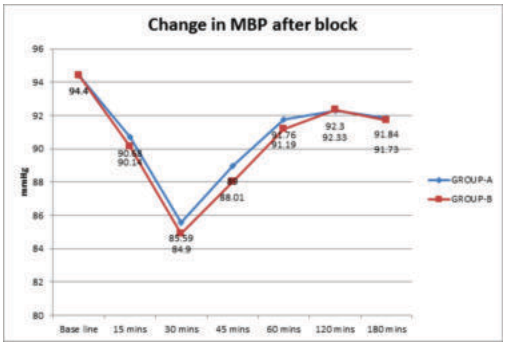


Pulse rate in beats/min was recorded at base line, 15 minutes, 30 minutes, 45 minutes, 60 minutes, 120 minutes and 180 minutes.

Base line pulse rate was comparable in both the groups with P Value of 0.40.

At 15 minutes, 30 minutes and 45 minutes, mean pulse rate were relatively low in Group B patients in respect to Group A and in each occasion they were statistically significant. At 60, 120 and 180 minutes, mean pulse rate were not significantly different in both the groups.

Diagram 3: Comparison of mean blood pressure between the two study groups:



At the start of the procedure, base line mean blood pressure (MBP) were comparable in both the groups with a P value of 0.99. After the procedure, MBP began to decrease in both the groups and this decrease was observed up to 45 minutes and it remained relatively low in Group B patients. When we compare the decrease in both the groups, the P values were not statistically significant.

Table 9: Change in systolic blood pressure (SBP) between two study groups:

SBP	STUDY GROUPS	N	Mean	Std. Deviation	P Value
Base line	GROUP-A	70	127.04	8.01	0.992
	GROUP-B	70	127.03	8.11	
15 minutes	GROUP-A	70	125.59	8.78	0.213
	GROUP-B	70	123.76	8.51	
30 minutes	GROUP-A	70	115.16	6.58	0.058
	GROUP-B	70	112.39	10.17	
45 minutes	GROUP-A	70	114.94	7.61	0.041
	GROUP-B	70	111.80	10.25	
60 minutes	GROUP-A	70	121.03	4.45	0.419
	GROUP-B	70	120.41	4.51	
120 minutes	GROUP-A	70	121.36	4.98	0.867
	GROUP-B	70	121.21	5.06	
180 minutes	GROUP-A	70	121.93	3.86	0.746
	GROUP-B	70	121.71	3.93	

At the start of the procedure, systolic blood pressure were comparable in both the groups with a P value of 0.992. After the procedure, SBP began to decrease in both the groups and this decrease was observed up to 45 minutes and it remained relatively low in Group B patients. When we compared the decrease in both the groups, the P values were not statistically significant except at 45 minute. At 45 minute, SBP was significantly lower in Group B patients.

Table 10: Change in diastolic blood pressure between two study groups:

DBP	STUDY GROUPS	N	Mean	Std. Deviation	P Value
Base line	GROUP-A	70	78.09	6.176	1.00
	GROUP-B	70	78.09	6.176	
15 minutes	GROUP-A	70	73.23	5.556	0.90
	GROUP-B	70	73.34	5.592	
30 minutes	GROUP-A	70	70.81	7.051	0.77
	GROUP-B	70	71.16	6.794	
45 minutes	GROUP-A	70	76.04	6.435	0.93
	GROUP-B	70	76.13	6.402	
60 minutes	GROUP-A	70	77.13	5.321	0.54
	GROUP-B	70	76.59	5.274	
120 minutes	GROUP-A	70	77.77	3.808	0.84
	GROUP-B	70	77.90	3.857	
180 minutes	GROUP-A	70	76.80	5.447	0.95
	GROUP-B	70	76.74	5.304	

At the start of the procedure, diastolic blood pressure were comparable in both the groups with a P value of 1.00. After the procedure, DBP began to decrease in both the groups and this decrease was observed up to 30 minutes and it remained relatively low in Group A patients. When we compared the decrease in both the groups, the P values were not statistically significant.

Table 11: Change in SPO2 between two study groups:

SPO2	STUDYGROUPS	N	Mean	Std. Deviation	P Value
Base line	GROUP-A	70	98.74	0.81	1.00
	GROUP-B	70	98.74	0.82	
15 minutes	GROUP-A	70	98.47	0.92	0.85
	GROUP-B	70	98.44	0.91	
30 minutes	GROUP-A	70	98.74	0.71	1.00
	GROUP-B	70	98.74	0.71	
45 minutes	GROUP-A	70	94.87	18.32	0.99
	GROUP-B	70	94.86	18.32	
60 minutes	GROUP-A	70	98.74	0.716	1.00
	GROUP-B	70	98.74	0.716	
120 minutes	GROUP-A	70	98.74	0.81	1.00
	GROUP-B	70	98.74	0.81	
180 minutes	GROUP-A	70	98.44	0.92	0.71
	GROUP-B	70	98.39	0.90	

Baseline SPO2 in both groups were comparable without statistical significance and it was maintained well without any significant change in both the groups during operation and in postoperative period.

Postoperative Care:

After the end of the surgery patients were sent to Post Anaesthetic Care Unit under the observation of a blinded resident who recorded for occurrence of any complication, time of appearance of first postoperative pain and time of recovery of complete motor functions of forearm and hand. Injection Tramadol 1.5mg per Kg body weight was given IV When VAS Score for pain was ≥ 4.

Occurrence of complication in two groups:

In Group-A, four patients and in Group-B seven patients developed bradycardia who were successfully managed with intravenous Atropine (0.6mg). Occurrence of bradycardia (Pulse rate <60/min) in two study groups was not statistically significant.

No patients developed significant hypotension, arrhythmia, pneumothorax or Horner's syndrome during observation period.

Discussion:

For upper limb surgeries brachial plexus block provide both intraoperative anaesthesia as well as postoperative analgesia and, it has an advantage over general anaesthesia like avoiding airway instrumentation, polypharmacy, decreased incidence of nausea and vomiting, early mobilisation and extended postoperative analgesia [6]. Of various approaches to brachial plexus, supraclavicular route is preferred as the narrowest part of plexus is located there and there will be rapid, dense and predictable anaesthesia of entire upper limb [8].

Dexmedetomidine is an alpha2 selective agonist. It acts in a manner similar to clonidine which is also an alpha2 selective agonist. Dexmedetomidine, the pharmacologically active d-isomer of

medetomidine is a highly specific and selective alpha2 adrenoceptor agonist with alpha2:alpha1 binding selectivity ratio of 1620:1 as compared to 220:1 for clonidine, thus decreasing the unwanted side effects of alpha1 receptors. One of the highest densities of alpha2 receptors has been located in the locus ceruleus. The hypnotic and sedative effects of alpha2-adrenoceptor activation have been attributed to this site in the CNS. It is also the site of origin for the descending medullospinal noradrenergic pathway, known to be an important modulator of nociceptive neurotransmission. In this region of the brain, alpha2-adrenergic and opioidergic systems have common effector mechanisms, indicating that dexmedetomidine has a supraspinal site of action. Presynaptic activation of alpha2 adrenoceptor in central nervous system (CNS) inhibits the release of norepinephrine, terminating the propagation of pain signals and their postsynaptic activation inhibits sympathetic activity, thereby decreasing HR and BP[9].

Singelyn et al. reported that a minimum dose of clonidine (0.5 mcg/kg) added to mepivacaine prolongs the duration of anaesthesia and analgesia after brachial plexus block. No added benefits were found with doses exceeding 1.5 mcg/kg. The enhancing effect of a small dose of clonidine on lignocaine may be because of the evoked inhibition of C-fibre action potential. Therefore, we decided to use clonidine at a dose of 1 mcg/kg in our study[10].

Karthik G. et al conducted a comparative study of dexmedetomidine (1mcg) and clonidine (1mcg) as adjuvants to levobupivacaine (0.5%) in supraclavicular brachial plexus block on fifty patients. They concluded that dexmedetomidine prolongs the duration of sensory and motor blockade enhancing the quality of block as compared to clonidine when used as adjuvant to levobupivacaine in supraclavicular brachial plexus block for upper limb orthopaedic surgeries. Duration of analgesia was significantly prolonged with dexmedetomidine thus making it a potential adjuvant for peripheral nerve blocks[11].

Although dexmedetomidine has an alpha2/alpha1 selectivity ratio that is eight-times higher than that of clonidine, an equipotent comparative study of both the drugs in peripheral nerve block was not available at the time of our study. The dose selection was based on previous studies where dexmedetomidine 1 mcg/kg and clonidine 1 mcg/kg were used in Bier's block as an adjuvant to lignocaine[12]. After literature review, we have found that dexmedetomidine and clonidine had peripheral action, which may be useful in using a lesser concentration of local anaesthetic (0.25%) to prolong the block with adequate anaesthesia. This in turn may be beneficial in high-risk patients.

The result of our study shows that all patients in both groups were comparable with respect to demographic profile and type of surgery. With the aforementioned doses, we had stable haemodynamics in all patients except lower pulse rate in Group B (dexmedetomidine) at 15, 30 and 45minutes as compared with Group A (clonidine). In Group-A, four patients and in Group-B seven patients developed bradycardia (<60 beats/min).

Esmaoglu A et al. added dexmedetomidine (100mcg) to levobupivacaine (0.5% 40ml) for axillary brachial plexus block and showed that it shortens the onset time of both sensory and motor block, prolongs the duration of block and the duration of post-operative analgesia[13]. In their study though onset of sensory and motor block onset time were shorter in Dexmedetomidine group, they were not statistically significant. In our study, we found that onset of sensory and motor block were faster with Group B as compared with Group A and it was statistically highly significant, the duration of analgesia in Group B was longer than in Group A, and it was statistically significant.

Feroz Ahmad Dar et al. evaluated the effect of adding dexmedetomidine to ropivacaine for axillary brachial plexus blockade in eighty patients scheduled for elective forearm and hand surgeries. Onset of sensory and motor block were shorter when dexmedetomidine was added, also sensory and motor blockade durations were longer along with duration of analgesia[14]. In our study also, we got similar effect when dexmedetomidine was added to levobupivacaine in supraclavicular brachial plexus block.

Conclusion and future scope:

We concluded that dexmedetomidine, when added to levobupivacaine in supraclavicular brachial plexus block has faster onset of sensory and motor blockade and prolonged duration of sensory and motor blockade compared to clonidine. Research is to be done in search of a suitable adjuvant to hasten the onset time and prolong the effect of the local anaesthetic with minimal side effect.

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Conflicts of interest: There are no conflicts of interest.

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