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Original article

COMPARISON OF DIFFERENT DOSE OF CLONIDINE AS ADJUVANT TO LOCAL ANAESTHETIC AGENT IN SUPRA CLAVICULAR BLOCK FOR POST OPERATIVE ANALGESIA

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ABSTRACT:

BACKGROUND:

supraclavicular bracheal plexus block(SBB) is used worldwide,for upper limb surgeries various adjuvant used to improve quality of the Anaesthesia as well as for increased duration of postoperative analgesia.

AIMS & OBJECTIVES:

:To access different dose of clonidine as adjuvant in SBB

MATERIAL & METHODS:

50 patients of ASA grade I or II, scheduled for upper limb surgeries, were randomly divided in two groups (A & B) of 25 each.

Supraclavicular brachial plexus block(SBB) performed with 20 ml lignocaine adrenaline 1.5%, 10 ml bupivacaine 0.5% and study drug in all patients.

Group A received 75 µg clonidine in 1 ml saline.

Group B received 150 µg clonidine in 1 ml saline.

Onset and duration of sensory and motor blockade was noted.

Patients were watched for intraoperative and postoperative side effects of drug, procedure related complications and hemodynamic alterations.

Duration of postoperative analgesia was interpreted by VAS score and noted in terms of first rescue analgesic needed.

OBSERVATIONS& RESULTS :

Demographics were comparable in both the groups.

time of onset for sensory block in Group B (6.04±0.93 min) was significantly lower than Group A (6.48±0.82 min).

Mean duration of sensory block was longer in Group B (9.66±1.59 hr) as compared to Group A (7.10±0.32 hr).

Mean onset time for motor block in Group B (11.24±1.01 min) was significantly lower than Group A (12.72±1.34 min).

Mean duration of motor blockade was longer in Group B (7.22±0.69 hr) as compared to Group A (5.32±0.36 hr).

Also, Duration of analgesia was significantly longer in Group B (11.7±1.61 hr) as compared to Group A (8.72±0.36 hr).

Preoperative & postoperative cardiorespiratory stability achieved in each group.

No any significant incidence of intraoperative or postoperative complication was observed in any group.

Conclusion: 150 mcg of clonidine is better adjuvant than 75 mcg for SBB.

INTRODUCTION:

Suraclavicular block is achieved by perineural introduction of local anaesthetic drugs, resulting in blockade of nerve impulses to abolish sensation. Local anaesthetics temporary terminate sensation from parts of body when injected in the vicinity of major nerve trunks. Brachial plexus blockade for upper limb surgery is the most common major peripheral nerve block technique.[28]Vasopressors and other drugs like opioids, alpha2 agonists , Tramadol, Fentanyl are used as adjuvant to local anaesthetics to enhance efficacy of local anaesthetic drugs and to maximize duration of the blockade. [16,17]Clonidine, a selective alpha2 adrenergic agonist with some alpha1 agonistic activity, when added to local anaesthetic solutions improved peripheral nerve blocks by reducing time of onset, improving the efficacy of the block during surgery, prolongation of anaesthesia and extending postoperative analgesia.[1,30]Clonidine possibly enhances sodium channel blockade action of local anaesthetics by opening up the potassium channels resulting in membrane hyperpolarization in which the cell is unresponsive to excitatory stimuli.[3]

Number of such studies has been carried out to study effects of clonidine as adjuvant to lignocaine, bupivacaine, ropivacaine or mepivacaine.[1,13,30] Dose dependent effects of clonidine in brachial plexus block have been also studied.[1,18]Our study is carried out to evaluate efficacy of two different doses of clonidine (75 and 150 µg) as adjuvant to supraclavicular brachial plexus block (20 ml lignocaine adrenaline 1.5%, 10 ml bupivacaine 0.5%) in adult patients (ASA grade I and II)

Onset time of sensorimotor blockage,Perioperative hemodynamic status,Duration of postoperative analgesia,Adverse effects of drug if any

Methods And Materials

We enrolled, after permission of institutional ethics committee, 50 patients of ASA grade I or II in the age group 25-50 years who are undergoing upper limb surgeries and divided them in two groups, A and B, with 25 patients each.

Exclusion criteria:

Allergic to study medications,History of significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal or hepatic disease.,Alcohol or drug abusers.,Pregnant or lactating mothers.,Patients on antiplatelet therapy,Local infection over supraclavicular area, bleeding diathesis.,Un-cooperative patientsPatients who refused for consent

Detailed pre anaesthetic check up was done in pre operative room or in ward day before surgery.Routine laboratory tests like haemoglobin, renal function tests, liver function tests, serum electrolytes, random blood sugar and chest x-ray were carried out.

Patients were explained about procedure in detail and written informed consent was obtained from each patient and relatives. They were explained about 6 hour fast prior to surgery. All Patients were also given instructions on how to measure pain with VAS (Visual Analogue Scale) 0-100 score, with 0 representing no pain and 100 representing worst pain.No patient received any sedative or narcotic premedication.

In operation theatre, routine monitors like ECG, pulse oximeter, NIBP cuff were applied and baseline pulse, BP, SPO_2 and respiratory rate were noted. Intravenous line was secured with 18G venous cannula and inj. ringer lactate was started. All patients were given inj. ondansetron 4 mg IV.

Brachial plexus block was performed with classic technique via supraclavicular approach. Patient was lied down in supine position with the head extended and turned toward contralateral side and ipsilateral arm was abducted.Under all strict aseptic precautions and sterile preparation of the supraclavicular area, a skin wheel was raised at the marked point with 1 ml of lignocaine 2%. A 23G-35mm insulated needle was inserted from the point 1 to 1.5 cm above The midpoint of clavicle and directed caudal, medial and posterior to locate brachial plexus with help of a peripheral nerve stimulator. The location end point was set by a distal motor response with an output lower than 0.9mA. After localization and negative aspiration of blood, study medications were given. Endtime of injection of drugs was considered as 0 min.

The patients were randomly divided into two groups. Patients in group A received 20ml 1.5% lignocaine with adrenaline (1:200,000), 10ml bupivacaine 0.5% and 75 µg of clonidine in 1 ml saline while those in group B received local anaesthetic with clonidine 150 µg in 1 ml saline.

The assessment for onset of sensory and motor block was done every minute from the time of injection of test drug until the block was established. Sensory block was evaluated by pinprick test in hand and forearm where as motor block was assessed by asking the patient to flex the forearm and hand against gravity,by modified bromadge score for upper limb.

Onset of sensory block was defined as the time elapsed between injection of drug and complete loss of pin prick sensation, while onset of motor block was defined as the time elapsed from injection of drug to complete motor block elicited as inability to move elbow, wrist and fingers. Only patients with complete motor block were included in the study.After the establishment of adequate sensorimotor block, surgery was started and time of beginning of surgery was noted. Intravenous fluids were continued intraoperatively at a rate of 2 ml/kg/hour. Intra operatively, pulse, BP, SPO_2 and ECG were monitored at 0, 15, 30, 60, 90, 120 and 150 minutes or up to duration of surgery, whichever was earlier. Any complication like tachycardia, bradycardia, hypotension, nausea, vomiting, breathlessness, cough, discomfort and sedation were noted.

Sedation level was assessed with Ramsay Sedation Scale (RSS) (19)at regular intervals same as hemodynamic parameters. The RSS scores sedation at six different levels, according to how arousable the patient is. Score of >3 was considered as sedation.(19)

All 50 patients were monitored for anaesthesia and analgesia up to 24 hr in the post-operative period.

- Duration of sensory block = time elapsed between injection of the drug and return of pinprick sensation
- Duration of motor block = time elapsed between injection of the drug to complete return of motor power evaluated by finger, forearm and shoulder movement. Intensity of postoperative pain was evaluated using VAS. Analgesia was considered satisfactory if the score was 30 or less. If the score was more than 30, analgesia was judged unsatisfactory and rescue analgesic inj. Diclofenac sodium 75mg IV was administered, 8 hourly thereafter. Time for first rescue analgesic was noted.

Postoperative vitals ,heart rate, blood pressure, respiratory rate, oxygen saturation and VAS were recorded at 0 min, 30 min, 1 hr, 2 hr, 3 hr, 4 hr, 6 hr, 9 hr, 12 hr and 24 hr. Arrival of patient to postoperative ward was considered as 0 min.

Patients were observed carefully for any complications of supraclavicular block like local hematoma, pneumothorax, local anaesthetic toxicity and side effects of clonidine like sedation, hypotension, bradycardia, nausea, vomiting etc.

TACYCARDIA was noted when pulse rate increased more than 20% of baseline value, and when declined more than 20% of baseline, it was labeled as BRADYCARDIA. Fall of more than 30% in systolic blood pressure and/or diastolic blood pressure were noted as HYPOTENSION. Hypotension es treated by inj.epherdrine6mg bolus& bradycardia by ink atropine IV In each patient, a chest x-ray was done 6 hrs postoperatively to rule out pneumothorax.NAUSEA VOMITING were assessed by point scale.In grade1/2 (no- mild form), ventimask oxygen & head low position given. Grade3/4 (moderate to severe form), pharmacological intervention in form of inj.ondansatron 4 mg given.Any transient neurological complications in early & late Postoperative period upto 72 hrs was noted.Data were presented as mean values and mean ± S.D and analyzed using unpaired t' test with p value <0.05 considered statistically significant. P values ≥0.05 were considered nonsignificant.

Observations and results

Table 1:Demographic Data

	Group A (n = 25)	Group B (n = 25)	P value	Inference
Sex (M/F)	19/6	19/6	≥0.05	NS
Age (Years)	33±6.5	33±5.7	≥0.05	NS
Weight (kg)	59±5.8	60±6.8	≥0.05	NS
Duration of surgery (min)	85.6±21.03	96.4±27.52	≥0.05	NS

Demographic Data was comparable in both groups.

Table 2:Onset of Anaesthesia

Onset	Group A	Group B	P value	Inference
Mean Sensory (min) Block	6.48±0.82	6.04±0.93	< 0.05	S
Mean Motor (min) Block	12.72±1.34	11.24±1.01	<0.05	S

Mean times of onset of sensory and motor block were significantly lower in group B.

Graph 1

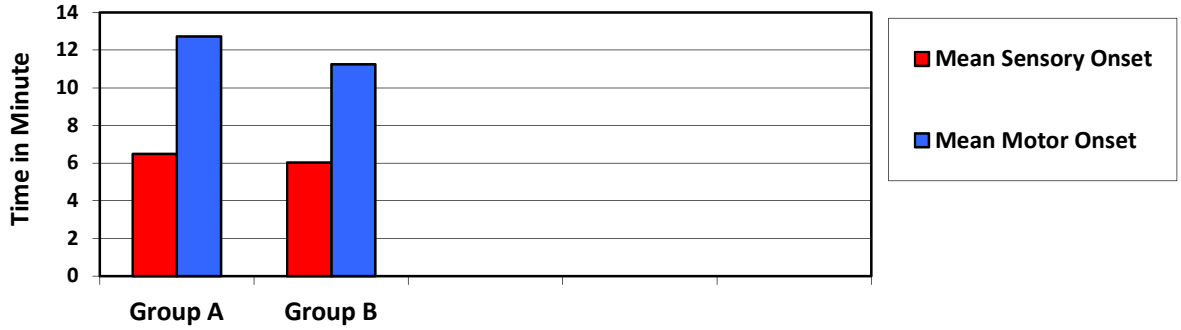
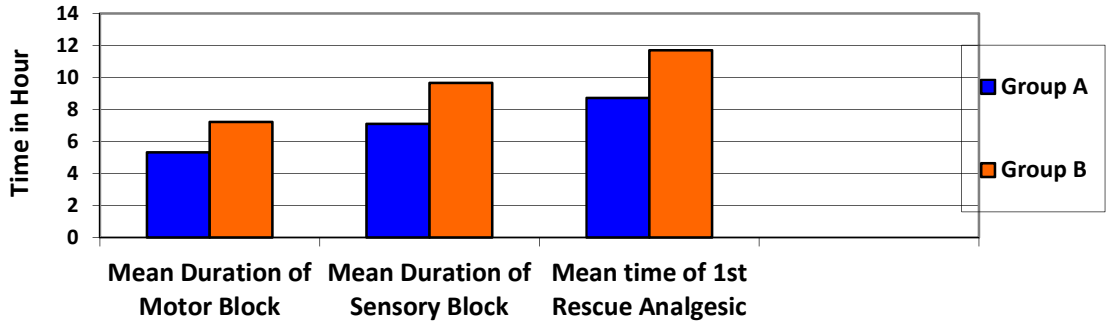


Table 3:Duration of Anaesthesia and Analgesia

Time(hrs)	Group A	Group B	P value	Inference
Mean duration of Motor Block	5.32±0.36	7.22±0.69	<0.05	S
Mean duration of Sensory Block	7.10±0.32	9.66±1.59	<0.05	S
Mean time of 1st rescue analgesic	8.72±0.36	11.7±1.61	<0.05	S

Graph 2



Mean Durations of motor and sensory block are significantly longer in Group B than in Group A.

Mean time for 1st rescue analgesic requirement for Group B is also longer than that in Group A.

Table 4:Intraoperative Pulse Rate and Respiratory Rate (p≥0.05)

Time (mins)	PULSE RATE (per min)		RESPIRATORY RATE (per min)	
	Group A	Group B	Group A	Group B
	Mean±S.D	Mean±S.D	Mean±S.D	Mean±S.D
0	85.36±7.04	85.32±7.13	15.24±0.93	15.28±0.98
15	82.64±6.26	84.08±5.99	15.40±0.71	15.36±0.91
30	84.40±6.58	84.08±7.43	15.48±0.92	15.44±1.00
60	78.80±4.80	78.56±6.96	15.52±0.82	15.40±0.82
90	79.46±3.67	73.58±15.79	15.69±0.63	15.21±0.92
120	82.00±3.46	76.17±11.60	16	14.83±0.98

Table 5:Intraoperative: Blood pressure (p≥0.05)

Time (min)	Group A		Group B	
	SBP(mmHg)	DBP(mmHg)	SBP(mmHg)	DBP(mmHg)
	Mean±S.D	Mean±S.D	Mean±S.D	Mean±S.D
0	123.44±8.52	78.32±5.40	122.16 ±7.26	77.64 ± 5.85
15	120.48±7.22	76.80±4.55	120.16±6.73	76.08±5.15
30	119.52±7.24	76.96 ±5.39	118.56± 7.36	75.12 ± 5.42
60	116.96±5.69	74±4.20	114.56±5.80	72.56 ± 5.36
90	115.38± 4.72	73.69±2.87	111.26± 5.45	69.78 ± 4.15
120	116±6.00	74.66±4.16	106.66 ± 7.65	69.66 ± 3.20

Table 6:Postoperative Pulse Rate and Respiratory Rate (p≥0.05)

Time	Pulse Rate (per min)		Respiratory rate (per min)	
	Group A	Group B	Group A	Group B
	Mean±S.D	Mean±S.D	Mean±S.D	Mean±S.D
0 min	85.12±6.53	86.00± 8.69	15.32 ± 1.03	15.32 ±1.03
30 min	84.40 ± 6.24	83.60 ±7.81	14.92 ±1.32	14.92 ±1.32

1 hr	84.48± 7.01	86.00 ± 8.06	14.88 ±1.30	14.88 ±1.30
2 hr	84.08±6.36	85.36±6.72	15.28 ±1.02	15.28 ±1.02
3 hr	84.16±6.45	84.24±6.00	14.84 ±1.28	14.84 ±1.28
4 hr	84.08±6.51	83.52±5.33	14.92 ±1.22	14.92 ±1.22
6 hr	84.24± 6.48	81.76±3.92	14.96± 1.207	14.96±1.20
9 hr	84.40±6.11	81.6 ±3.95	14.96±1.06	14.96±1.66
12 hr	86.24± 6.11	81.36±4.68	14.84± 0.98	14.84 ±0.98
24 hr	86.64±6.21	81.44±4.30	14.88±1.05	14.84±1.11

Table 7:Postoperative Blood pressure (P > 0.05)

Time	Group A		Group B	
	SBP(mmHg)	DBP(mmHg)	SBP(mmHg)	DBP(mmHg)
	Mean±S.D	Mean±S.D	Mean±S.D	Mean±S.D
0 min	121.12±7.83	78.56±4.38	122.08±8.65	76.66±6.39
30 min	119.48±8.24	78.6 ±3.94	126.85±8.62	81.4 ±6.31
1 hr	118.44±6.51	78.48±4.09	122.28±8.69	75.71±4.85
2 hr	117.68±6.09	79.6 ±3.87	118±7.07	73.76±4.59
3 hr	118.52±5.32	80.52±3.56	118.14±6.28	71.7±4.21
4 hr	118.68±5.20	80.68±3.74	120.28±5.54	73.14±4.21
6 hr	119.28±6.64	82.24±3.87	119.71±4.94	72.5 ±3.40
9 hr	122.32±7.11	83.72±8.00	120 ±5.41	72.85±3.65
12 hr	124.16±6.07	83.12±3.40	118.28±4.12	73.42±3.40

24 hr	126.16±6.85	84.52±3.55	116.96±2.84	74.72±2.70

Perioperative Hemodynamic and respiratory parameters were comparable in both groups throughout the study period.

Table 8: perioperative Complications:No any incidence of nausea, vomiting, hypotension or tachycardia was observed in any group.No any procedure related complications like hematoma, pneumothorax or neurological sequale were noted in any patient. Bradycardia (fall >20% from baseline pulse) occurred in one patient of Group B which was clinically not significant and did not require any treatment.

RSS score was comparable throughout the study period. Intraoperative RSS score was >3 in 2 patients in Group A and in 4 patients in Group B but no any incidence of decline in SpO2 was noted.No need of airway intervention in any patients.

Discussion

Supraclavicular approach to brachial plexus block involves injection of local anaesthetic around the divisions of the brachial plexus deep to the prevertebral fascia posterolateral to subclavian artery. Due to compact arrangement of all three trunks of plexus in this region, this block provides complete regional anaesthesia for surgeries on the distal arm, elbow, forearm, wrist or hand.[8]Clonidine exerts an analgesic effect and enhances peripheral nerve blocks of local anaesthetics by selectively blocking conduction of A-δ and C fibres. It casuses hyperpolarization by increasing sodium and potassium conductance across neural cell membrane. Clonidine also thought to cause local vasoconstriction, thereby reducing the vascular uptake of local anaesthetics.[24]

Demographics were comparable in both the groups. Duration of surgery in Group A was **85.6±21.03** min and **96.4±27.52** min in Group B ($p \geq 0.05$).

Onset of Motor and Sensory blockade: Mean onset of sensory block in Group A was **6.48±0.82** min and **6.04±0.93** min in Group B. Mean onset of motor block was noted at **12.72±1.34** min in Group A and **11.24±1.01** min in Group B.Kohli S et al[18] found a faster onset of sensorimotor block in patients who received higher dose.

JM et al[1] concluded in the study that sensory blockade was more pronounced and faster in the groups receiving 30, 90 or 300 µg of clonidine compared to lignocaine used alone for axillary brachial plexus block.

Chakrabati S et al[6] mentioned that time of onset of surgical block was about 7 min faster in 30 µg clonidine adjuvant group as compared to bupivacaine alone in supraclavicular block.

Patil KN et al[22] observed early onset of sensorimotor block when clonidine 1 μg/kg was used with ropivacaine in supraclavicular block compared to control group.

Duration of Motor and Sensory blockade:

In our study, the mean duration of motor block was found to be **5.32±0.36** hour in Group A and **7.22±0.69** hour in Group B. While the mean duration of sensory block was **7.10±0.32** hr in Group A and **9.66±1.59** hr in group B. Durations of both sensory and motor block were significantly longer in Group B patients who received higher (150 μg) dose of clonidine (p value <0.05).Kohli S et al[18] concluded that duration of sensorimotor blockade was longer in group II (2 μg/kg) than in group I (1 μg/kg).Bernard JM et al[1] tested three doses over a 10-fold range (30, 90, 300 μg) as adjuvant to 1% lignocaine in axillary block and observed that each dose of clonidine extends the sensory block and duration prolongs with increasing doses.Singelyn FJ et al[30] in their study of 7 different doses of clonidine in brachial plexus block concluded that there is a significant linear increase in the duration of anaesthesia in doses up to 0.5 μg/kg. Results of our study are comparable to above studies.

Duration of Postoperative Analgesia:

Perception of postoperative pain was recorded by VAS score. Before the start of procedure, all patients At regular intervals in postoperative period they were asked to point out the perception of pain on this scale. The duration of analgesia was recorded up to the time of need for rescue analgesic when VAS score was above 30. Mean duration of 1st rescue analgesic was **8.72±0.36** hour postoperatively in Group A and **11.7±1.61** hour in Group B, which was significantly longer in Group B compared to Group A (p<0.05).Our results run parallel to many studies that show, prolongation of postoperative analgesia with the use of clonidine in brachial plexus block depends on dose of clonidine.Bernard JM et al[1] while studying dose range effects of clonidine in brachial plexus block concluded that time elapsed before the first supplemental analgesic showed significant relationship to the dose of clonidine. Higher doses results in more prolongation of the analgesic effects that follows neural blockade.Buttner J et al[4] concluded dose-dependent prolongation of analgesia with significant difference between all the groups. Kohli S et al[18] specifically compared 1 μg/kg and 2 μg/kg doses of clonidine for postoperative analgesia and found a longer duration of analgesia in terms of delayed requirement of first rescue analgesic with 2 μg/kg dose group.Singelyn FJ et al[30] compared a wide range of clonidine doses in their study and observed that 0.1 μg/kg dose increases duration of analgesia significantly over control group. Duration of analgesia in 0.5, 1 and 1.5 μg/kg doses showed statistically significant difference when compared to groups with 0.1-0.4 μg/kg doses.

Perioperative Hemodynamic and Respiratory stability: One patient from group B had decrease in pulse rate >20% from baseline, but was not significant clinically otherwise all patients were vitally stable.

S et al[18] while studying sixty patients with clonidine in supraclavicular block, observed a stable hemodynamics (HR, MAP, SpO_2) in most of the patients both intraoperatively and postoperatively. (One episode of bradycardia, no hypotension with 1 μg/kg dose and two bradycardia, one hypotension with 2 μg/kg dose.)

Patil KN et al did not observe any significant fluctuation in pulse rate and mean arterial pressure.

Singelyn FJ et al concluded with increasing doses of clonidine (0.1-1.5 μg/kg). Neither hypotension nor bradycardia was noted in any group.

Duma A et al showed that with 150 μg clonidine as adjuvant stable vitals were there.

All the above studies support our results of study and confirm that clonidine in doses up to 150 μg can be used without significant hemodynamic or respiratory instability.

Adverse effects and complications: Main side effects associated with use of clonidine are bradycardia, sedation and hypotension. In our study, we did not observe inraoperative or postoperative hypotension and bradycardia. Only a single event of clinically non-significant bradycardia was recorded. 2 patients in group A and 4 patients in group B had intraoperative RSS score of 4 (>3 RSS was defined as sedation) but that was not associated with any decrease in SpO_2. Highest peak in mean RSS score was seen at 60 min intraoperatively in both the groups without any intergroup difference. Complications which may occur due to technique of supraclavicular brachial plexus block are pneumothorax, haematoma and neural damage.Intraoperatively or postoperatively no any complication was noted in any group.Bernard JM et al[1] observed that patients who received 300 μg were more sedated than those who received 90 μg along with fall in SpO_2 in 4 out of 14 patients.McCartney CJ et al[20] in their review study concluded that side-effects appear to be limited at doses up to 150 μg. Duma A et al[9] did not observe any significant difference in sedation score with or without clonidine.Our findings run parallel to these studies and conclude that 150 μg clonidine can be used in brachial plexus block with minimal undesirable side effects.

Conclusion : Clonidine in different doses hastens onset of neural blockade, prolongs duration of sensorimotor blockade and provides longer postoperative analgesia with minimum hemodynamic disturbances. Compared to 75 μg, 150 μg of clonidine with local anaesthetics provides prolong motor and sensory analgesic effect in supraclavicular brachial plexus block.

In nutshell, clonidine as 150 µg dose can be used effectively and safely with local anaesthetic agents for brachial plexus block via supraclavicular approach for various upper limb surgeries.

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