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A Randomized Controlled Study of The Efficacy of Addition of Clonidine to Bupivacaine as Compared with Bupivacaine Alone used in Supracalvicular Brachial Plexus Block for Upper Limb Surgeries

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Abstract

Introduction: Regional nerve blocks of the upper extremity avoid the polypharmacy and stress of laryngoscopy and tracheal intubation associated with general anaesthesia. Drug administration at the supraclavicular level offers comprehensive anaesthesia for the complete limb. Post-operative analgesia may be provided by either adding additives to the local anaesthetics or placing a catheter in place. Clonidine (alpha 2 adrenergic receptor agonist) is a classic additive to local anaesthetic in various regional procedures.

Aim: To compare efficacy of clonidine added as an adjuvant to bupivacaine with plain bupivacaine alone in supraclavicular brachial plexus block.

Methodology: Fifty ASA I and II patients coming for upper limb surgeries were assigned randomly into two equal groups.

Group S: received 35 ml of 0.25% Bupivacaine and 0.5 ml of normal saline 0.9%.

Group C: received 35 ml of 0.25% Bupivacaine and Clonidine 75mcg (0.5 ml).

Onset and duration of sensory and motor blockade and complications, if any were documented.

Results: Demographic variables were comparable. There was a statistically significant faster onset and prolonged duration of block in clonidine group when compared to plain bupivacaine ($p<0.05$). Clonidine also produced sedation which however did not require any clinical intervention.

Conclusion: We conclude that clonidine causes earlier onset, prolongs the duration of sensory and motor block with sedation and without any significant clinical side effects when added to bupivacaine in brachial plexus block.

Keywords: Bupivacaine; Clonidine; Brachial plexus block.

Introduction

Supraclavicular Brachial plexus block is the standard regional anaesthesia technique of the upper limb. This is due to the excellent surgical anaesthesia and effective postoperative pain relief it offers. A variety of additives have been fount not only improve the efficacy of the blockade but also reduces the total local anaesthetic dosage.[1,2,3,4] Clonidine has been studied as an additive over a wide dose range.[5] Hence we undertook this study to analyse the efficacy of clonidine as an additive to local anaesthetic in supraclavicular brachial plexus block.

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Aim

To compare efficacy of clonidine added as an adjuvant to bupivacaine with plain bupivacaine alone in supraclavicular brachial plexus block.

Primary outcome:

- Duration of analgesia

Secondary outcome:

- Onset of sensory blockade
- Onset and duration of motor blockade
- Hemodynamic parameters
- Sedation score

Methodology

After obtaining Institutional Ethical committee clearance and written informed consent, fifty patients in the age group of 18 to 60 years were included in the study. Orthopedic procedures of the upper limb were planned to be done under supraclavicular brachial plexus block. Any hypersensitivity to the drugs under study and contraindication to blocks were excluded. The participants were randomized based on computer generated random numbers into two groups.

Group S (25 each) – 35 ml of 0.25% Bupivacaine with 0.5 ml of normal saline.

Group C (25 each) – 35ml of 0.25 % Bupivacaine with 75mcg of clonidine (0.5 ml).

A pilot study was conducted in 10 patients with 5 in each group. The mean difference in the duration of analgesia was found as 105 minutes with a confidence interval of 95% and 80% power of the study. A sample size of 23 in each group was considered adequate. An anaesthesiologist not involved in the study opened the sealed envelope and prepared the drug solution as per the randomization while the anaesthesiologist performing the procedure was blinded to the allotted group. Patients were shifted to the operation theatre, standard monitors attached and baseline parameters noted. Intravenous access with an 18 G IV cannula on the non-surgical limb was secured. The patient was placed in supine position with the head turned away from the side to be blocked. The surgical arm is adducted and the supraclavicular area is prepared aseptically. A 22 gauge needle was introduced in the parasagittal plane at the superior border of the clavicle at the lateral edge of the sternocleidomastoid muscle insertion. The response to nerve stimulator was noted. Twitch of pectoralis, deltoid, biceps (upper trunk), triceps (upper and middle trunk) and hand (lower trunk) muscles with current intensity of 0.4 mA was done. Distal responses (hand or wrist flexion or extension) were accepted as confirmed placement within the fascia. Anaesthetic solution was injected while the needle was fixed in position. Onset of sensory block was defined as the time elapsed between injection of drug and complete loss of pinprick sensation of the hand, while onset of motor blockade was defined as the time elapsed from injection of drug to complete motor block. Duration of sensory block (the time elapsed between injection of drug and appearance of pain requiring analgesia) and duration of motor block (the time elapsed between injection of drug and complete return of muscle power) would also be recorded.

Ramsay sedation Score

1. Anxious and agitated or restless or both.
2. Cooperative, oriented and tranquil.
3. Responding to commands only.
4. Brisk response to light glabellar tap.
5. Sluggish response to light glabellar tap.
6. No response to light glabellar tap.

The hemodynamic parameters and sedation scores were assessed at 5, 10, 20, 30, 60 min and later on at 120,240,360, 480, 540 and 600 minutes.

Results

Demographic variables were comparable as shown in Table 1. Group C had faster sensory (6.60±2.386 minutes) and motor onset (9.80±2.693 minutes) than Group S ($p < 0.05$ Fig 1). The mean duration of sensory blockade was 505.20 ± 50.010 minutes in Group C and 333.96 ± 63.16 in Group S. The difference was highly significant (Table 2). The mean duration of motor block was 294.80 ± 49.508 minutes in group S while Group C showed 414.60 ± 52.335 minutes and this too was statistically significant (Table 2). There was a significant difference in the mean duration of analgesia with group S showing 356.00 ± 52.994 minutes in comparison to group C which showed 527.20 ± 51.358 minutes (Fig 2). Mean heart rate was significantly lower in group C than in Group S during observation period of 15 min to 360 mins (Fig 3). There was no significant fall in systolic or diastolic blood pressure during the observation period in the groups (Fig 4 and 5).

Sedation score

The sedation score in Group S was 1 in all the patients throughout the period of observation. In group S, majority of the participants scored 2 in the sedation scale from 15th minute after injection till two hours. This change reverted back to score 1 at 360 minutes of observation. No patient crossed sedation score of 2 and above during the study period. Statistical analysis of sedation score showed that the difference was significant ($p < 0.05$) (Table 3).

Table 1: Demographic Data.

	Group I (n=25)	Group II (n=25)
Sex(M/F)	18(72%) /7(28%)	14(56%) /11(44%)
Age (in Years)	36.96 ± 11.995	40.76 ± 8.781
Weight (in kg)	65.40 ± 5.986	57.56 ± 5.432

Table 2: Comparison of DOB in Sensory and Motor.

	Group	N	Mean	SD	t Test	P Value
DOB Sensory	Group I	25	333.96	63.169	10.627	0.000
	Group II	25	505.20	50.010		***
DOB Motor	Group I	25	294.80	49.508	10.189	0.000
	Group II	25	441.60	52.335		***

Table 3: Comparison of Sedation Score.

Sedation Score	Score	Group I	Group II	Chi Square Test	P Value
0	1	25(100)	25(100)	NA	NA
	2	–	–		
5	1	25(100)	25(100)	NA	NA
	2	–	–		
10	1	25(100)	24(96)	1.02	0.312
	2	0(0)	1(4)		NS
15	1	25(100)	7(28)	28.125	0.000
	2	0(0)	18(72)		***
30	1	25(100)	2(8)	42.593	0.000
	2	0(0)	23(92)		***
60	1	25(100)	6(24)	30.645	0.000
	2	0(0)	19(76)		***
120	1	25(100)	6(24)	30.645	0.000
	2	0(0)	19(76)		***
240	1	25(100)	15(60)	12.500	0.000
	2	0(0)	10(40)		***
360	1	25(100)	22(880	3.191	0.074
	2	0(0)	3(12)		NS
480	1	25(100)	25(100)	NA	NA
	2	0(0)	0(0)		
540	1	25(100)	25(100)	NA	NA
	2	0(0)	0(0)		
600	1	25(100)	25(100)	NA	NA
	2	0(0)	0(0)		

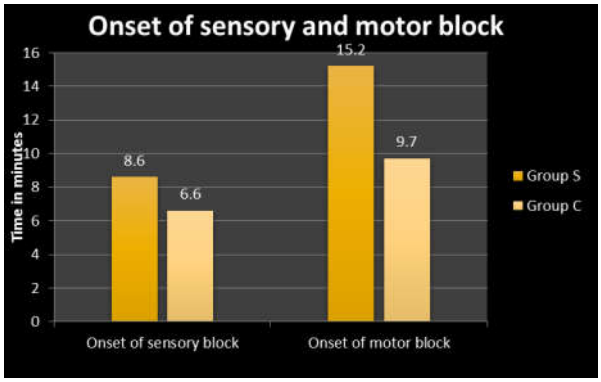

Fig 1: Comparison of Onset of sensory and motor block.

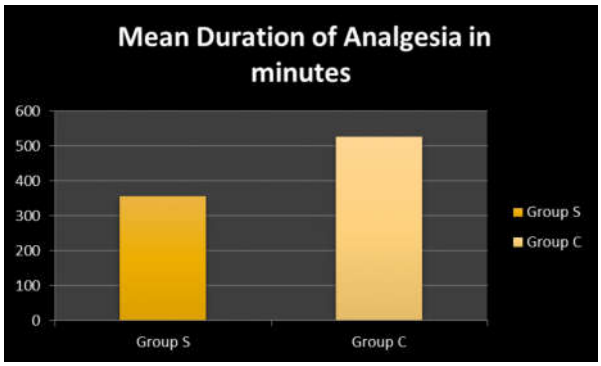

Fig 2: Comparison of Duration of analgesia.

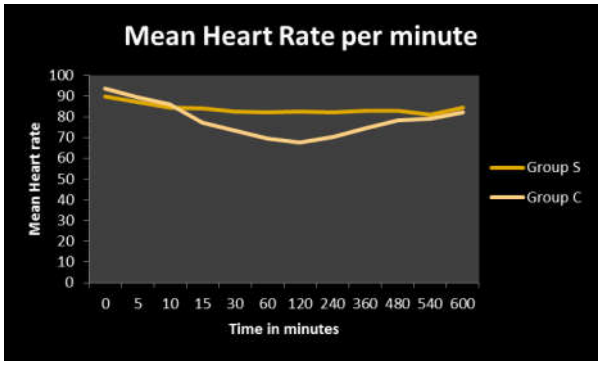

Fig 3: Comparison of Mean Heart rate per minute.

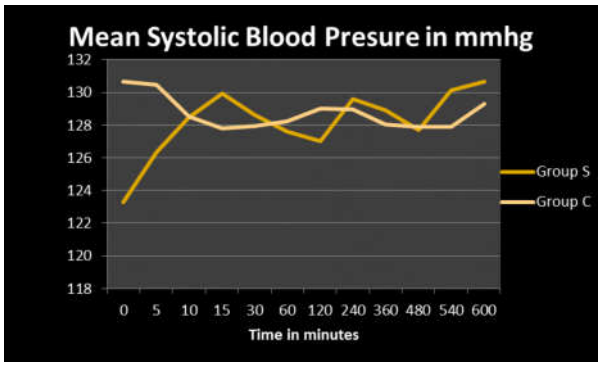

Fig 4: Comparison of Mean Systolic blood pressure in mmhg per minute.

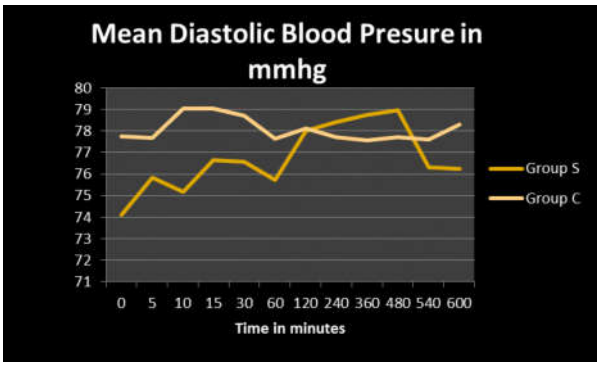

Fig. 5: Comparison of Mean Diastolic blood pressure in mmhg per minute.

Discussion

Bupivacaine is the most frequently used local anaesthetic due to its relatively longer duration of action which ranges from 3 to 8 hours.[6] The prominent shortcoming of Bupivacaine is its long onset time in regional blocks. On mixing short and long acting local anaesthetics, researchers found that even though the onset time was shortened, the duration of the blockade was reduced as the total effective concentration of bupivacaine was less.

Various studies have investigated several adjuncts including opioids, midazolam, neostigmine, hyaluronidase and bicarbonate,[1,2,3,4] but the results have been inconclusive with either ineffective outcomes or higher incidence of adverse effects and their limitations.

Limited studies are available on the effects of clonidine on the analgesic property of local anaesthetic agents in peripheral nerve blocks.[7–15] Previous studies have proved that clonidine hydrochloride which is an imidazole derivative, known to produce antinociception, enhances the effect of local anaesthetics when administered intrathecally and epidurally. It is proved that a very low dose of clonidine increased the C-fibre blockade from lignocaine induced blockade as shown in an isolated de-sheathed rabbit vagus nerve.[16]

This study was carried out in Fifty ASA I and II patients in SRM Medical College undergoing elective upper limb surgery. We had equal number of study population in both the groups. Both the groups received equal amounts of the local anaesthetic solution with the group S receiving 0.5 ml of normal saline and group C receiving 75 mcg of clonidine. A nerve stimulator was used to improve the precision and success rate of the blockade. Variables related to sensory and motor blockade, hemodynamic parameters and sedation scores were compared.

In our study, the clonidine group had a faster onset of both sensory and motor blockade compared to the other group. Clonidine and local anaesthetic agents have a synergistic action. Clonidine enhances both sensory and motor blockade of neuraxial and peripheral nerves by the local anaesthetic solution. This is thought to be due to blockage of conduction of A-delta and C fibers, increased potassium conductance observed in isolated neurons in vitro and intensification of conduction block achieved by local anaesthetics.

Our study showed a significantly longer mean duration of sensory and motor blockade was achieved by the clonidine group as compared to the control group (Table 3). This concurs with the results of the study done by Cucchiaro G[11] and colleagues in children where they demonstrated prolongation of the duration of sensory block with the use of clonidine.

Iskandar H et al[8] and Iohom G et al[10] too showed that the sensory blockade in the clonidine group were longer when compared to the control groups. The equivalent results between our study and by previous investigators could be due to the similar methodology applied and the near similar drug regimens used. In contrast, Duma A et al[17] and Culebras X et al[18] showed that there was no added advantage in terms of duration of blockade between the clonidine and placebo group. They concluded that addition of Clonidine produced a variable, inconsistent and unpredictable effect.

In our study we observed a significant prolongation in the mean duration of analgesia in the clonidine group than in the control group. McCartney and colleagues found that clonidine used as an adjunct to bupivacaine prolonged the postoperative analgesic effects compared to bupivacaine alone when administered for various peripheral nerve blocks.[12]

Popping DM et al[14] too showed that the difference in duration of postoperative analgesia for the clonidine group was significantly higher than the control group. This prolongation in the duration of blockade was attributed the interaction between clonidine and the axonal ion channel and its receptors. The mechanism of action is inhibition of the action potential of A and C fibers in the peripheral nerves by clonidine.

Our study showed that there was significant prolongation of mean duration of motor blockade in the clonidine group compared to the control

group. Popping DM[14] in his study showed that there was significant prolongation of the average duration of motor blockade by 141 minutes when clonidine was used as an adjuvant.

This was further concurred by Cucchiaro G[11] and colleagues. In contrast to this Duma[17] and colleagues showed that clonidine did not prolong the duration of block. The reasons for this inconclusive result have been discussed.

In our study we found out that there was a reduced pulse rate of patients in group C. Significant changes in heart rate occurred after 15 min and was maintained till 360 minutes. Even though some patients had minimal decrease in systolic, diastolic as well as the mean arterial pressure all of them maintained their hemodynamic parameters within the normal range. There was no significant hemodynamic change that had to be interfered with other drugs. It has been observed in few studies that intravenous and neuraxial administration of clonidine resulted in significant hemodynamic variations including bradycardia and hypotension.[18]

Intraoperative sedation scores were higher in clonidine group when compared with the control group which was statistically significant. However, none of the patients had any episodes of desaturation.

Conclusion

Addition of 75mcg of clonidine to bupivacaine causes a faster onset of sensory and motor block and prolongs the duration of analgesia without producing any clinically significant adverse effects in supraclavicular brachial plexus blocks.

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References

1. Keeler JF, Simpson KH, Ellis FR, Kay SP. Effect of addition of hyaluronidase to bupivacaine during axillary brachial plexus block. Br J Anaesth 1992; 68:68–71.
2. Bazin JE, Massoni C, Bruelle P, Fenies V, Groslier D, Schoeffler P. The addition of local anaesthetics in brachial plexus block: The comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia 1997;52:858.
3. Bone HG, van Aken H, Brooke M, Burkle H. Enhancement of axillary brachial plexus block anaesthesia by coadministration of neostigmine. Reg Anesth Pain Med 1999;24:405–10.
4. Jarbo K, Batra YK, Panda NB. Brachial plexus block with midazolam and bupivacaine improves analgesia. Can J Anesth 2005; 52: 822 – 826.
5. Bernard JM, Macaire P: Dose-range effects of Clonidine added to Lignocaine for brachial plexus block. Anaesthesiology 1997; 87:277–84.
6. Butterworth JF, Strichartz GR. Molecular mechanisms of local anesthetics. A review. Anesthesiology 1990; 72: 711–25.
7. El Saied AH, Steyn MP, Ansermino JH. Clonidine prolongs the effect of Ropivacaine for axillary brachial plexus blockade. Can J Anaesth 2000; 47: 962–7.
8. Iskandar H, Benard A, Ruel-Raymond J, Cochard G, Manaud B: The analgesic effect of interscalene block using Clonidine as an analgesic for shoulder arthroscopy. Anesth Analg 2003; 96:260–62.
9. Hutschala D, Mascher H, Schmetterer L, Klimscha W, Fleck T, Eichler H.G, Tschernko EM. Clonidine added to bupivacaine enhances and prolongs analgesia after brachial plexus block via a local mechanism in healthy volunteers. European Journal of Anaesthesiology 2004; 21(3):198–204.
10. Iohom G, Machmachiv A, Deśire´ PD, Khatouf M, Boileau S , François DF. The Effects of Clonidine Added to Mepivacaine for Paronychia Surgery Under Axillary Brachial Plexus Block. Anesth Analg 2005;100:1179–83.
11. Cucchiaro G, Ganesh A. The Effects of Clonidine on Postoperative Analgesia After Peripheral Nerve Blockade in Children. International Anaesthesia Research Society March 2007; 104(3):240–45.
12. McCartney CJ, Duggan E, Apatu E. Should we add clonidine to local anesthetic for peripheral nerve blockade? A qualitative systematic review of the literature. Reg Anesth Pain Med 2007; Jul-Aug, 32(4):330–8.
13. YaDeau JT, LaSala VR, Leonardo P, Kahn RL, Kethy MJ, Levine DS, Clonidine and Analgesic Duration After Popliteal Fossa Nerve Blockade: Randomized, Double-Blind, Placebo-Controlled Study. Anesth Analg, June 2008; 106(6):120–130.
14. Popping DM, Elia N, Marret E, Wenk M, Trame MR. A Meta-analysis of Randomized Trials. Clonidine as an Adjuvant to Local Anesthetics for Peripheral Nerve and Plexus Blocks. Anesthesiology Aug 2009; 111(2):321–26.
15. Chakraborty S, Chakraborty J, Mandal MC, Hazra A, Das S. Effect of Clonidine as adjuvant in Bupivacaine induced supraclavicular brachial plexus block - lled trial. Indian Journal of Pharmacology. Apr 2010; 42(2): 74 –77.
16. Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effects of Lidocaine on C-Fiber action potential. Anesth Analg 1992; 74 (5): 719–725.

17. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S: Clonidine as an adjuvant to local anaesthetic axillary brachial plexus block: A randomized, controlled study. Br J Anaesth 2005; 94:112–116.

18. Culebras X, Van Gessel E. Clonidine combined with a long acting local anesthetic does not prolong postoperative analgesia after brachial block but does induce hemodynamic changes. Anesth Analg 2001; 92: 201–04.