Original Research Article

Comparative study of effect of clonidine 0.5 mcg/kg and 1 mcg/kg as an adjuvant to 0.5 % bupivacaine in Ultrasound guided supraclavicular brachial plexus block

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Abstract

Background: The most preferred anaesthetic technique for upper limb surgeries is the Brachial Plexus Block under Ultrasound Guidance. Clonidine, potentiates peripheral nerve blocks by reducing the time of onset, improving the efficacy of the block during surgery and extending postoperative analgesia. The most optimal dose of clonidine in peripheral nerve blocks is still unclear. **Objectives:** To compare the onset and duration of sensory and motor blockade between 0.5 mcg/kg and 1 mcg/kg of clonidine used as an adjuvant to the local anaesthetic agent (0.5% bupivacaine) in ultrasound guided supraclavicular brachial plexus block in patients undergoing upper limb surgeries and adverse effects. **Methodology**: A double blinded Comparative study was done among patients scheduled for upper limb surgeries under supraclavicular brachial plexus block at Department of Anesthesia, Sri Manakula Vinayagar Medical College and Hospital, Puducherry during October 2016 to May 2018. 66 patients who fulfilled the inclusion and exclusion criteria in each group were allotted to either of the group(33 in each) by Systematic Random Sampling. The hemodynamic parameters were measured and different durations. Time of onset of sensory and motor blockade and time of rescue analgesia were noted. Post-operative analgesia was also assessed. **Results:** There is no significant difference in heart rate, Systolic Blood Pressure, Diastolic Blood pressure and Mean arterial Pressure at different time points between both the groups. Mean time of onset of Motor(9.5 Vs 6.0 min) and Sensory(10.7 Vs 5.6) blockade was found to be less among Group B participants as compared to that of Group A. Duration of motor (487 Vs 588) and sensory blockade(514 Vs 665) and the time for requirement of first rescue analgesia(514 Vs 665) was found to be high among Group B participants as compared to that of Group A.
Key Word: bupivacaine.

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INTRODUCTION

The most preferred anaesthetic technique for upper limb surgeries is the Brachial Plexus Block.[1] Regional anaesthesia is a safe, low cost technique that provides prolonged postoperative pain relief, avoids untoward effects of anaesthetic drugs, upper airway manipulation and instrumentation. [2,3] This technique is superior to the conventional blind nerve localisation technique. It provides accuracy and reduces the volume of drug to be injected and avoids complications like arterial puncture, nerve damage and pneumothorax.[4] Numerous drugs have been studied for their usage as adjuvants to local anaesthetic agents for enhancing their effects including morphine, pethidine, clonidine, dexmedetomidine, butorphenol and buprenorphine out of which clonidine emerged as one of the successful agent.[5-7] Clonidine, an imidazoline, with selective partial agonist activity at α2 adrenergic receptor, potentiates peripheral nerve blocks by reducing the time of onset, improving the efficacy of the block during surgery and extending postoperative analgesia. Many studies have shown that clonidine promotes

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faster onset of action of the local anaesthetic agent and prolongs the analgesic effect.[9] So far smaller doses are found to be more beneficial than higher doses. The most optimal dose of clonidine in peripheral nerve blocks is still unclear.[2,8] Hence this study was conducted to compare the efficacy of two different doses (0.5 mcg/kg versus 1mcg/kg) of clonidine as adjuvant to 0.5% bupivacaine in ultrasound guided supraclavicular brachial plexus block in upper limb surgeries.

OBJECTIVES

To compare the onset and duration of sensory and motor blockade between 0.5 mcg/kg and 1 mcg/kg of clonidine used as an adjuvant to the local anaesthetic agent (0.5% bupivacaine) in ultrasound guided supraclavicular brachial plexus block in patients undergoing upper limb surgeries and adverse effects.

MATERIALS AND METHODS

A Comparative study was done among patients scheduled for upper limb surgeries under supraclavicular brachial plexus block at Department of Anesthesia, Sri Manakula Vinayagar Medical College and Hospital, Puducherry during October 2016 to May 2018. Institutional ethical committee approval was obtained and 66 patients who consented for the study were randomly allotted to either of the group through Systematic Random Sampling. Group A (n=33) received 0.5 mcg of clonidine and Group B (n=33) received 1 mcg of clonidine as adjuvant to 0.5% Bupivacaine. The sample size was calculated using Open Epi software, considering the mean onset of motor block between two groups : 13.2 +/- 6.7 and 18.5 +/- 7.8 as proposed in a previous study by Kaur et al[10] at 95% of confidence interval and 80% power. Considering 10% non response rate, total same size of 66 with 33 in each group was arrived. Patients who had chronic pain and on analgesics, taking other adrenergic blockers, anticoagulants, history of brachial plexus injury, previous upper limb surgeries, deformity/congenital anomaly of upper limbs, bilateral upper limb pathologies, local site infection, allergy to the drugs that are tested or any other contraindications for regional anaesthesia, alcoholics, Drug abusers and Pregnant / Lactating women were excluded from the study. Patients in both the groups received ultrasound guided supraclavicular brachial plexus block performed by a board certified qualified and licensed anaesthetist. Vital parameters (Electrocardiogram, Non invasive Blood pressure, Heat Rate, peripheral oxygen saturation) were monitored before and throughout the procedure. An intravenous line was secured on the opposite limb and intravenous fluid was started. The patient and the anaesthesiologist were both blinded to the group. Under strict aseptic precautions, the block was performed with a 22 gauge 50 mm short bevelled echogenic needle for optimal control and visibility under undersound system (Sonosite M-Turbo).Successful block was assured when at least two out of four nerve territories – radial, median, ulnar and musculocutaneous nerves –were effectively blocked according to Vester-Andersen's criteria. Sensory and Motor blockade was assessed after the injection every 5 minutes for the first 20 mins then at 30 mins, 1 hr, 2 hrs and thereafter every 2 hrs till 8 hrs and at the 12th hr. Sensory blockade was assessed by pinprick test and scored according to a three point scale in the four dermatomes.

Score 2: sharp pain;
Score 1: blunt pain;
Score 0: no pain

The onset of sensory blockade was defined as a score of 1 in at least two of the four nerve territories. Time of onset of
sensory blockade and time of rescue analgesia were noted. Injection tramadol 50 mg intramuscular was given as rescue
analgesia. The duration of the sensory blockade was observed from the onset to the time of rescue analgesia or a score
2 in any of the four territories of the nerve. Post-operative analgesia was assessed at the same time intervals as sensory
blockade using visual analogue scale.

STATISTICAL ANALYSIS

Data was entered in Microsoft Excel and analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions and their association was tested using chi square test. Continuous variables were represented as mean and standard deviation and comparison of means was done by independent sample 't' test. Mann Whitney U test was applied to test the statistical difference when the data was non-normally distributed. P value of <0.05 was considered as statistically significant.

RESULTS

Both the study groups were comparable in terms of age (p value -0.284), gender distribution (p value -0.618), BMI (p value – 0.849), baseline heart rate (P value – 0.511), Systolic Blood pressure (P value – 0.892), Diastolic blood pressure (P – 0.217) and Mean Arterial Pressure (P value – 0.560). Hence both the groups are comparable with respect to all basic parameters. There is no significant difference in heart rate, Systolic Blood Pressure, Diastolic Blood pressure and Mean arterial Pressure at different time points between both the groups. (Table 1) Mean time of onset of Motor and Sensory blockade was found to be less among Group B participants as compared to that of Group A. Duration of motor and sensory blockade and the time for requirement of first rescue analgesia was found to be

high among Group B participants as compared to that of Group A. All the values were statistically significant (P<0.0001). (Table 2) Statistically significant Lower scores of Post-operative analgesia was observed in Group B as compared to that of Group A study participants at 5 and 10 mins intervals. Though there was no statistically significant difference at other time intervals. (Table 3) Significantly lower sedation scores were observed in Group B study participants as compared to that of Group A participants throughout the observation. (Table 4)

Table 1: Comparison of Mean/Median Heart rate, Systolic Blood Pressure, Diastolic Blood Pressure and Mean Arterial Pressure between both groups

Time Interval	Heart rate			Systolic blood pressrure			Diastolic blood pressure			Mean arterial pressure		
	Mean/Median		P	Median		P	Mean/Median		P	Mean		P
	Group A	Group B	value	Group A	Group B	value #	Group A	Group B	value	Group A	Group B	value *
Before	78	71	0.511#	119	120	0.892	67	70	0.217# 0.317#	86.1	87.2	0.560
5 mins	75.79	73.7	0.384*	118	120	0.919	67	69		85.8	86.5	0.729
10 mins	75.8	73.7	0.4*	119	121	0.666	67	70	0.267#	85.4	86.7	0.501
20 mins	76	73.7	0.343*	119	120	0.893	68.7	70.4	.0524*	85.6	86.8	0.540
30 mins	76	73.7	0.344*	118	120	0.758	67	69	0.258#	85.4	86.4	0.568
60 mins	76	73.7	0.358*	119	120	0.928	67	69	0.325#	85.5	86.4	0.646
120 mins	75.7	73.4	0.374*	117	120	0.671	67	69	0.342#	85.2	86.3	0.532
240 Mins	75.7	73.5	0.356*	118	120	0.681	68.7	69.8	0.658*	85.4	86.4	0.598
360 Mins	75.9	73.8	0.382*	119	121	0.607	68.9	69.8	0.712*	85.6	86.5	0.637
480 Mins	76	73	0.572#	118	120	0.990	68.9	69.8	0.703*	85.6	86.4	0.676
720 Mins	76.1	73.8	0.342*	117	120	0.714	68.5	70	0.532*	85.2	86.5	0.522

* Independent sample t test was applied ;# Mann Whitney U test was applied to test the statistical difference between the two groups since the data was non- normally distributed.

Table 2: Comparison of mean onset time and duration of motor and sensory blockade

	Group A (n = 33)		Group B (n = 33)		Difference in	P Value*
	Mean	SD	Mean	SD	mean	
Time of onset of motor blockade(min)	9.5	2.0	6.0	1.99	3.5	0.0001
Duration of motor blockade(min)	487	9.8	587.9	12.9	99.2	0.0001
Time of onset of sensory blockade(min)	10.7	0.9	5.6	1.1	5.1	0.0001
Duration of sensory blockade(min)	514.1	25.7	665	26.1	150.9	0.0001
Time for requirement of first rescue analgesia(min)	514.1	25.7	665	26.1	150.9	0.0001

*Independent Sample student t test was applied for comparison of means

Table 3: Distribution of study groups based on post operative analgesia score at various time intervals

Time interval	Score	Group A N(%)	Group B N(%)	P Value *
5 minutes	**1**	0(0.0)	9(27.3)	
	2	6(18.2)	21(63.6)	
	3	27(81.8)	3(9.1)	<0.001
10 minutes	**0**	1(3.0)	1(3.0)	
	1	19(57.6)	19(57.6)	

	2	13(39.4)	13(39.4)	0.011
15 minutes	0	22(66.7)	24(72.7)	0.592
	1	11(33.3)	9(27.3)	
480 minutes	0	22(66.7)	25(75.8)	
	1	11(33.3)	8(24.2)	0.415
720 minutes	**1**	5(15.2)	15(45.5)	
	2	23(69.7)	13(39.4)	0.020
	3	5(15.2)	5(15.2)	

* *Chi Square test was applied to test statistical difference in proportions*

Table 4: Distribution of study groups based on sedation score at various time intervals

Time interval	Score	Group A N(%)	Group B N(%)	P Value *
10 minutes	**3**	0(0.0)	3(9.1)	
	4	9(27.3)	18(54.5)	
	5	24(72.7)	12(36.4)	0.007
15 minutes	**3**	0(0.0)	18(54.5)	
	4	30(90.9)	15(45.5)	
	5	3(9.1)	0(0.0)	<0.001
20 minutes	**2**	0(0.0)	3(9.1)	<0.001
	3	0(0.0)	27(81.8)	
	4	33(100.0)	3(9.1)	
30 minutes	**2**	0(0.0)	3(9.1)	<0.001
	3	0(0.0)	30(90.9)	
	4	33(100.0)	0(0.0)	
60 minutes	**2**	0(0.0)	3(9.1)	<0.001
	3	3(9.1)	30(90.9)	
	4	30(9.9)	0(0.0)	
120 minutes	**3**	0(0)	33(100.0)	<0.001
	4	33(100.0)	0(0)	
240 minutes	**3**	3(9.1)	33(100.0)	<0.001
	4	27(81.8)	0(0.0)	
	5	3(9.1)	0(0.0)	
360 minutes	**3**	0(0.0)	27(81.8)	<0.001
	4	30(90.9)	6(18.2)	
	5	3(9.1)	0(0.0)	
480 minutes	**4**	9(27.3)	33(100.0)	<0.001
	5	24(72.7)	0(0.0)	

* Chi Square test was applied to test statistical difference in proportions

DISCUSSION

With the advancement of technology, the regional anaesthesia techniques have been refined over the years with the help of multiple instrumental discoveries. They have become the most preferred mode of anaesthesia in most of the Orthopaedic surgeries and the technique is found to be safe, well tolerated and provides a reliable block even in the elderly and children.[11] Post operative pain is a main concern in orthopaedic surgeries or in any upper limb surgery and hence the need to prolong the duration of the nerve blockade provided by the local anaesthetic was studied using various medications as adjuvants which could be added to the local anaesthetic solution.[7] Brachial plexus blocks have become the standard technique of anaesthesia for all surgeries being performed in the upper limb as it provides more patient comfort and is better acceptability.[12] Ultrasound imaging aids in clear localisation of the brachial plexus and also reduces the number of needling attempts. Also, it helps in the visualisation of the spread of the drug inside the sheath of the nerve bundle.[13] Clonidine, which is an alpha – 2 adrenergic agonist, has been extensively studied for its effect of prolonging the duration of anaesthesia while added to local anaesthetics in peripheral nerve blocks.[14,] But still the correct dose with minimal side effects that can be administered is still under research. Current study was carried out to compare the efficacy of 0.5mcg/kg and 1 mcg/kg clonidine with 0.5% Bupivacaine. Blocks were administered under ultrasound guidance and no case of failure of block was observed. The two groups were comparable in terms of age (p value = 0.284), gender (p value= 0.618) and BMI (p value = 0.849). The systolic, diastolic and mean arterial blood pressures at various time intervals intra and post operatively were not significantly different between the two groups (p value >0.001) at all instances. In the current study, the mean time of onset of motor blockade was 9.5 ± 2.0 mins in group A and 6.0 ± 2 mins in group B with the differences in mean being statistically significant (p<0.001). The mean duration of motor blockade was 487.1 ± 9.8 mins in group A and 587.9 ± 12.9 in group

B with the differences in mean being statistically significant (p<0.001). Hence it was inferred that group B had early onset time and longer duration of motor blockade. Similarly with respect to sensory blockade the mean time of onset being 10.7 ± 0.9mins in group A and 5.6 ± 1.1 mins in group B. The mean duration of sensory blockade was 514.1 ± 25.7mins in group A and 665 ± 26.1mins in group B. The differences of both the means were statistically significant (p<0.001). Group B had lesser time for onset and had longer duration of sensory blockade. Since the time of rescue analgesia was considered corresponding to the end point of sensory blockade, it was also clear that group B took significantly longer time than group A to require rescue analgesia. Also, group B had significantly lower post operative analgesia scores than group A at the first 5 and 10 minutes but with progression of time, both the groups had comparable scores. The sedation scores were significantly lower in group B than group A starting at 10 mins and lasting till 480 mins (p<0.001). The incidence of other side effects like bradycardia, hypotension, nausea and dizziness was nil in both the groups. The patients who received 0.5 mcg/kg of clonidine had significant prolongation of blockade with literally no other side effects. This inference was re enforced by results of an earlier study conducted by Francoise J Singelyn et al[27] The patients who received 1 mcg/kg of clonidine had a higher incidence of sedation which lasting for approximately 8 hrs which could be beneficial during the intra operative period as inferred by multiple studies that were done earlier. The findings of the studies conducted by Shivinder Singh and Amitabh Aggarwal,[15] Jean-Marc Bernard and Philippe Macaire[16] and Susmita Chakraborty et al,[17] comparing the effect of plain local anaesthetic agents versus added clonidine on peripheral nerve blocks, were all in accordance with our result of increased sedative effect of clonidine at higher doses. kaur et al[10] compared 1 mcg/kg and 2 mcg/kg (group 1 and group 2) of clonidine and reported that 2 mcg/kg of clonidine provided longer duration of blockade with higher incidence of side effects like sedation, bradycardia and hypotension. The values of onset times and duration of the sensory and motor blockade of our study were more or less comparable to the findings to their study. As well as, other aspects of this study were found to be in accordance with the results of our study. At a dose of 1 mcg/kg, we were able to achieve adequate amount of post operative analgesia along with sedation and no observed haemodynamic changes which made it the most preferable dose for administration as an adjuvant to local anaesthetic in supraclavicular blocks. However, we propose that additional caution be undertaken while using clonidine as an adjuvant in peripheral nerve blocks, as inadvertent intravascular administration can worsen the local anaesthetic systemic toxicity that presents as a result, since clonidine further deranges the haemodynamics by causing bradycardia and hypotension.

CONCLUSION

Both 0.5 mcg/kg and 1 mcg/kg of Clonidine provided comparable post op analgesia when added as an adjuvant along with 0.5% Bupivacaine in Ultrasound guided Supraclavicular Brachial Plexus Block with no significant hemodynamic changes or side effects. However 1 mcg/kg provided an earlier onset and longer duration of sensory and motor blockade with increased sedation, and less side effects. 1mcg/kg of clonidine can be recommended as the ideal dose to be administered along with local anaesthetics in peripheral nerve blocks.

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