Hemodynamic stability after bupivacaine alone and with clonidine, fentanyl and midazolam additives in brachial plexus blockade: A comparative study

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Abstract Background: Bupivacaine is markedly cardiotoxic. Certain drugs such as clonidine, fentanyl and midazolam have been used as adjuncts to local anesthetics to lower the dose of each agent and enhance the efficacy of the blockade while reducing the incidence of adverse effects of each of the agents. Aim: To compare the hemodynamic stability after bupivacaine alone and with clonidine, fentanyl and midazolam additives in brachial plexus blockade. Material and Methods: This prospective randomized comparative study included 60 adult patients undergoing upper limb surgeries. Baseline vital signs were recorded and monitored every 5 mins till the procedures was over and thereafter every hour for 24 hours. Results: Hemodynamic variables like pulse rate, blood pressure was found to altered much in group BC than group BF and group BM, during the first 30 mins of the intraoperative period. But no patient required vasopressor support. Conclusion: Hemodynamic parameters were found to be altered much in bupivacaine and clonidine combination than the other groups.

Keywords: Brachial plexus blockade, bupivacaine, clonidine, fentanyl, midazolam, hemodynamic stability

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INTRODUCTION

Brachial plexus block was found to provide excellent pain control, less side effects, and lower levels of postoperative pain when compared with general anesthesia.¹ Various additives are added to local anaesthetic agents which along with complete pain relief and total muscle relaxation, it produces vasodilatation,

which improves blood circulation and prevents tissue hypoxia.² Bupivacaine is markedly cardiotoxic. It binds specifically to the myocardial proteins. In toxic concentrations the drug decreases the peripheral vascular resistance and myocardial contractility producing hypotension and possible cardiovascular collapse. Certain drugs such as clonidine, fentanyl and midazolam have been used as adjuncts to local anesthetics to lower the dose of each agent and enhance the efficacy of the blockade while reducing the incidence of adverse effects of each of the agents.³⁻⁷ Fentanyl also have been successfully used as adjuvants to local anesthetics in brachial plexus block.³ Clonidine improves the quality and the duration of the local anesthetic nerve blocks as well as in spinal and epidural anesthesia.8 This property has been attributed to the fact that $\alpha 2$ adrenergic agonists enhance the nerve block of local anesthetics by facilitation of C fiber blockade, by local vasoconstriction or by spinal action caused by diffusion along the nerve or

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retrograde axonal transport. Midazolam is known to produce antinociception and to enhance the effect of local anaesthesia when given epidurally or intrathecally.⁹ This study was carried out with the objective of comparing the hemodynamic stability after bupivacaine alone and with clonidine, fentanyl and midazolam additives in brachial plexus blockade.

MATERIAL AND METHODS

This prospective randomized comparative study included 60 adult patients undergoing upper limb surgeries at the Department of Orthopedics and Department of Plastic Surgery of a tertiary care teaching hospital over a period of two years. The study was commenced after receiving the approval from institutional ethical committee. Informed consent was taken from all the patients.

Inclusion criteria

- Both sexes
- ASA I and II.
- Age Group 20-60 years
- Weight 40-70 kgs
- Surgeries of the upper limb.

Exclusion Criteria

- Patients refusal
- Coagulopathy
- Infection at injection site

All included patients were randomly allocated into 4 groups brachial plexus block with Nerve Stimulator was performed with supraclavicular block technique. Study groups:

- 1. BC group: 15 patients received 30ml of 0.25% Bupivacaine with 1mcg/kg of preservative free Clonidine to the maximum of 75 mcg.
- 2. BF group: 15 patients received 30ml of 0.25% Bupivacaine with preservative free Fentanyl 1 mcg/kg to the maximum of 50 mcg.
- 3. BM group: 15 patients received 30ml of 0.25% Bupivacaine with preservative free Midazolam 50 mcg/kg.
- 4. B group: 15 patients received 30ml of 0.25% Bupivacaine.

Methodology

Patients were all pre-operatively evaluated, clinically examined and investigations done prior to assessment Procedures were explained in detail and written consent obtained. Initially the pre procedure parameters were recorded i.e., pulse rate, blood pressure, SPO2, ECG. Then block was administered. All through the study,

these parameters were monitored continuously except the NIBP which was recorded intermittently. Post-operatively they were monitored for 24 hours. Patients were observed vigilantly for development of various complications. The skin and subcutaneous tissue was infiltrated with local anaesthetic solution. The subclavian artery was palpated above the medial third of the clavicle. A 35mm 21G insulated needle was attached to the nerve locator set at 1-5mA and inserted through the weal created in downward, inward and backward direction, so that it was pointing to the spine of second to fourth thoracic vertebra. The superior trunk of the brachial plexus was usually located first. The needle position was adjusted while decreasing the current to 0.9mA with maintenance of the muscle response. The response that results in the greatest block success was muscle contraction below the shoulder. A cough from the patient is a warning sign that the pleura is being contacted by the needle. Incremental injection of local anaesthetic was made with repeated aspiration. After injecting the local anaesthetic the block was tested for both sensory (using pin prick) and motor (using muscle power) and is compared with same stimulation or power in the contralateral arm. Motor block was evaluated by thumb abduction (Radial nerve), thumb adduction (Ulnar nerve), thumb opposition (Median nerve) and flexion of the elbow in supination and pronation of the forearm (Musculocutaneous nerve). The Hollmen's scale was used in the study for assessing both sensory and motor blockade. Evaluation was carried out for every minute after completion of injection and the time of onset was noted both for sensory and motor blockade. Onset of blockade both sensory and motor was defined as a minimum of grade 2 in Hollmen's scale. Block was considered complete when sensory and motor scores were at least grade 3 in Hollmen's scale. Only patients with complete block were included in the study. Baseline vital signs were recorded and monitored every 5 mins till the procedures was over and thereafter every hour for 24 hours. Onset, completion of blockade, duration of blockade was assessed. Pain was assessed using visual analog scale (VAS).

Statistical analysis

Quantitative variables were compared by mean and standard deviation, using Independent sample t-test. Categorical variables were compared by using Chi square test. P value < 0.05 was considered as statistically significant.

C Suganthalakshmi

RESULTS

In our study, all the study groups were comparable in terms of baseline characteristics such as age, gender distribution, type of cases taken up for surgery.

Table 1: Demographic profile of the patients in study groups								
Characteristics	Group BC	Group B	F Group BM	Group B				
Age group								
20-25 yrs	04	06	02	01				
26-35 yrs	04	02	06	04				
36-45 yrs	01	02	02	05				
46-55 yrs	03	05	03	03				
56-65 yrs	03	00	02	02				
Sex								
Male	10	12	10	10				
Female	05	03	05	05				
1_{-}	4521654	421 ± 6.54	1 222+6.54					

Duration of sensory block was 602±6.54, 452±6.54, 421±6.54 and 332±6.54 min in group BC, BM, BF and B respectively. The duration of motor block was 557.3±7.24, 414±7.24, 389±7.24 and 292±7.24 min in group BC, BM, BF and B respectively.

Table 2: Onset and duration of	sensory and mot	tor block in stu	ıdy groups	
Onset and duration of sensory and motor block	Group BC	Group BF	Group BM	Group B
Sensory block				
Onset Mean±SD (min)	4.73±0.19	6.46±0.19	5.8±0.19	7.6±0.19
Duration Mean±SD (min)	602±6.54	452±6.54	421±6.54	332±6.54
Motor block				
Onset Mean±SD (min)	6.26±0.25	7.73±0.25	7.73±0.25	10.13±0.25
Duration Mean±SD (min)	557.3±7.24	414±7.24	389±7.24	292±7.24

Hemodynamic variables like pulse rate, blood pressure was found to altered much in group BC than group BF and group BM, during the first 30 mins of the intraoperative period. But no patient required vasopressor support. The hypotension was only mild and corrected only with intravenous crystalloids.

	Table 3: Hemodyna	mic variables i	n all study gro	lins	
Variables		Group BC	Group BF	Group BM	Group B
Pulse rate 15mins	Mean	78.06667	86.0667	83.93333	82.53333
	Standard Error	1.94463	1.94463	1.94463	1.94463
	Probability Level	0.036908 Significant			
	Mean	77.06667	85.4	83.4	81.6
Pulse rate 30mins	Standard Error	1.83541	1.83541	1.83541	1.83541
	Probability Level	0.015791 Significant			
Systolic BP 15mins	Mean	122.0667	128.2	132	128.6667
	Standard Error	2.790858	2.790858	2.790858	2.790858
	Probability Level	0.098164 Significant			
Systolic BP 30mins	Mean	118.3333	128.3333	130.7333	126.9333
	Standard Error	2.646321	2.646321	2.646321	2.646321
	Probability Level	0.009869 Significant			
Diastolic BP 15mins	Mean	77.93333	82.6	82.4	81.33334
	Standard Error	1.666	1.666	1.666	1.666
	Probability Level	0.180946 Significant			
Diastolic BP 30mins	Mean	76.46667	82.4	81.6	79.53333
	Standard Error	1.442	1.442	1.442	1.442
	Probability Level	0.024695 Significant			

DISCUSSION

The supraclavicular block of the brachial plexus is a useful alternative to general anesthesia for upper limb surgeries as they provide reliable and ideal operating conditions by maintaining stable hemodynamics, superior analgesia, and muscle relaxation. Clonidine activates central α -2 adrenergic receptors in medullary vasomotor centre which inhibits the release of norepinephrine from the adrenergic neurons and reduces sympathetic outflow from the central nervous system. Further there is reduced

discharge from the post ganglionic fibers of cardiac nerves and an increase in parasympathetic tone. This results in decrease in blood pressure, heart rate, cardiac output, peripheral vascular resistance. Nucleus tractus solitarius, the site that modulates the autonomic control including vagal activity is an important central site for the action of clonidine. Reduction in sympathetic tone is accompanied by lowering of plasma renin activity, decrease in renal vascular resistance and maintenance of renal blood flow even when the blood pressure is lowered. Vasopressor centers of the brainstem retain their sensitivity to baroreceptor control and hence postural hypotension is considerably less than the effects of drugs that act on the autonomic ganglia and peripheral adrenergic receptors. The absence of fall in blood pressure when clonidine is given to tetraplegic with complete spinal cord transection above the level of sympathetic outflow also suggests a central site of hypotensive action.9 Fentanyl has no action on cardiac contractility but cause hypotension in large doses due to bradycardia, venodilation and suppression of central sympathetic out flow.¹⁰ Midazolam decreases peripheral vascular resistance and alter baroreceptor reflexes transiently leading to hypotension and tachycardia. In hypovolemic and elderly patients there is increased risk of significant hypotension.¹¹ In our study, hemodynamic variables like pulse rate, blood pressure was found to altered much in group BC than group BF and group BM, during the first 30 mins of the intraoperative period. But no patient required vasopressor support. The hypotension was only mild and corrected only with intravenous crystalloids. Hrishi *et al*¹² studied efficacy of clonidine as an additive on the duration of action of brachial plexus block performed under ultrasound and nerve locator guidance and found that none of the patients in study group had significant hemodynamic changes from the baseline recording. Even though some patients had a minimal decrease in systolic, diastolic as well as the mean arterial pressure, all of them maintained their hemodynamic parameters within the normal range. Laiq et al compared the hemodynamic stability of supraclavicular block with bupivacaine alone and bupivacaine-midazolam combination and found that blood pressure, heart rate, respiratory rate and oxygen saturation remained stable throughout the procedure and postoperatively as they did not differ significantly during the study period.13

CONCLUSION

Hemodynamic parameters were found to be altered much in bupivacaine and clonidine combination than the other groups.

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