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A CLINICAL COMPARATIVE STUDY BETWEEN BUPIVACAINE-CLONIDINE COMBINATION AND BUPIVACAINE (PLAIN) IN BRACHIAL PLEXUS BLOCK BY SUPRACLAVICULAR APPROACH

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ABSTRACT

Background and objectives : Adjuncts to local anaesthetics for brachial plexus block may enhance the quality and duration of analgesia. Clonidine, an Alpha-2 adrenergic agonist, is known to produce antinociception and enhance the effect of local anaesthetics when given epidurally, intrathecally or in various peripheral nerve blocks. The purpose of this study was to assess the effect of Clonidine added to brachial plexus block by supraclavicular approach. **Methods :** A prospective, randomized, single blinded study was conducted on 60 ASA I or II adult patients undergoing upper limb surgeries under supraclavicular brachial plexus block. Patients were randomly divided into two groups. Patients in Group B (n = 30) were administered 25mL of 0.5% Bupivacaine and Group BC (n = 30) were given 25mL of 0.5% Bupivacaine with Clonidine 1µg/kg. The onset time and duration of sensory and motor blockade were recorded. Haemodynamic variables (i.e., heart rate, noninvasive blood pressure, oxygen saturation), sedation scores and rescue analgesic requirements were recorded for 24 hrs postoperatively. **Results :** The onset of sensory and motor block was significantly faster in Group BC compared to Group B ($P < 0.05$). Rescue analgesic requirements were significantly less in Group BC compared to Group B ($P < 0.05$). Haemodynamics and sedationscores did not differ between groups in the post-operative period. **Conclusion :** Clonidine (1µg/kg) in combination with 25mL of Bupivacaine (0.5%) hastened onset of sensory and motor block, and improved postoperative analgesia when used in brachial plexus block, without producing any adverse events.

Keywords: Supraclavicular brachial plexus block; Clonidine; Bupivacaine

1.INTRODUCTION

Brachial plexus blocks provide a useful alternative to general anaesthesia for upper limb surgeries. They achieve near ideal operating conditions by producing complete muscular relaxation, maintaining stable intra-operative hemodynamics and the associated sympathetic block. The sympathetic block decreases post-operative pain, vasospasm, and edema.

Of various local anesthetics, bupivacaine is used most frequently as it has a longer duration of action varying from 3 to 8 hours. However, there are many limiting factors like delayed onset, patchy or incomplete analgesia, short duration etc.

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Various drugs like neostigmine, opioids, hyaluronidase, midazolam etc.[1-3] have been added to local anaesthetics in order to modify the block in terms of quick onset, good quality, prolonged duration and post-operative analgesia. But these presented with adverse systemic effects or doubtful efficacy.

Clonidine, an imidazoline alpha-2 adrenergic receptor agonist mainly used as an anti-hypertensive agent. Alpha-2 receptors mediate sedation, analgesia, and sympatholysis. Clonidine is known to produce anti-nociception and enhance the effect of local anaesthetics when given intrathecally, epidurally and in peripheral nerve blocks. Clonidine produces this effect by modulating pain pathways through receptors. It also produces sedation through acting on pontine locus ceruleus where highest density of alpha-2 receptors are present. Neuraxial placement of clonidine inhibits spinal substance P release and nociceptive neuron firing produced by noxious stimulation.

So the present study is being undertaken in a randomized single blinded manner to evaluate the onset time, duration and analgesic efficacy of clonidine-bupivacaine(0.5%) combination compared to plain bupivacaine (0.5%) for brachial plexus block by supraclavicular approach.

2.MATERIALS AND METHODS

Sixty patients aged 18 to 55 years, scheduled for elective orthopedic operations in the upper limb, under supraclavicular brachial plexus block, were included in this study. They were of American Society of Anesthesiologists (ASA) Grade I or II physical status. The procedures were of moderate duration and included implant removal, both bone plating, fixation of lower third of humerus and olecranon fixation. Patients receiving chronic analgesic therapy, those with severe cardiopulmonary disease, thyroid disorders, diabetes mellitus, central or peripheral neuropathies, history of allergy to local anesthetics, or other contraindications to regional anesthesia were excluded from the study.

Randomization and Blinding

The study was designed as a prospective, randomized, single-blind, study. Participants were allocated to two equal groups of 30 each. Group BC patients received 25 ml of 0.5% bupivacaine and (1 mcg/kg) clonidine, while group B received 25 ml of 0.5% bupivacaine in supraclavicular approach for brachial plexus block. All observations (hemodynamic variables, oxygen saturation, level of sedation, time required to achieve surgical block in the operation theater and the time to rescue analgesic in the postanesthesia care unit) were also recorded in a blinded manner

INTERVENTIONS

Once a patient was brought in to the operation theatre standard monitoring was set up, including noninvasive arterial blood pressure, heart rate, and pulse oximetry. An 18-gauge IV cannula was inserted in the forearm and an infusion started

with lactated Ringer's solution. Midazolam 0.05 mg/kg IV bolus was used for sedation after the block was achieved, so as to allay apprehension and anxiety during the operative procedure. The surgical procedure was performed by using a standard arm tourniquet inflated to 70 mmHg higher than systolic blood pressure. Hemodynamic variables were measured 10 min before block placement and every 3 min thereafter till the end of surgery.Patient lies supine, arms by the side and head turned slightly to the other side.The interscalene groove and mid-point of clavicle would be identified. After aseptic preparation of area, at a point 1.5 to 2.0cm posterior and cephalad to mid point of clavicle, subclavian artery pulsations are felt. A skin wheel is raised. With local anaesthetic just cephalo-posterior to the pulsations.Next, a 22 gauge, 5 cm needle, mounted on a 20 ml syringe, would be passed through the same point, parallel to the head and neck, in a caudad, slightly medial and posterior direction, until either paraesthesia was elicited or first rib was encountered. If the first rib is encountered, the needle would be moved over the first rib until a paraesthesia was elicited either in the hand or arm.After eliciting paraesthesia and negative aspiration of blood, the study medication would be injected.All patients would be monitored for anaesthesia and analgesia upto 24 hours post-operatively.Sensory block was evaluated by temperature testing using spirit soaked cotton on skin dermatomes C4 to 12 where as motor block was assessed by asking the patient to adduct the shoulder and flex the forearm against gravity.

Onset of sensory block was defined as the time elapsed between injection of drug and complete loss of cold perception of the hand, while onset of motor blockade was defined as the time elapsed from injection of drug to complete motor block.Sedation score described by University of Michigan Sedation Scale(UMSS) would be used to assess sedation.1 - Awaked & Alert. 2 - Minimally Sedated: tired/sleepy, responding to verbal stimulus. 3-Moderatly Sedated: somnolent/sleeping, responding to mild physical stimulus. 4-Deeply Sedated: deep sleep, responding to moderate to severe physical stimulus. 5- Unarousable. Heart rate, non-invasive blood pressure and O_2 saturation were also monitored. 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.IM injection of Diclofenac sodium would be given as rescue analgesic when patients complains of pain. Number of rescue analgesics in 24 hours of post-operative period would also be recorded. All patients were clinically assessed during discharge from the orthopedic ward and again after 3 weeks (at the first routine postoperative examination) for occurrence of any neurological complications. All 30 patients in the two groups were considered for adverse event analysis. However, subjects who failed blocks were excluded from effectiveness assessment

3.RESULTS

Sixty ASA I and II of either sex aged between 18 - 55 years, posted for upper limb surgeries under supraclavicular brachial plexus block were selected for the study.

The study was undertaken to evaluate the efficacy of Clonidine (1µg/kg) as adjuvant to Bupivacaine (0.5%) in comparison with plain Bupivacaine (0.5%) for brachial plexus block by supraclavicular approach.

Table 1:Age distribution study

Study group	Mean ± SD (min)	Mean difference	t* value	P value	Significance
B	33.5±10.64	8.7	0.754	0.454	NS
BC	31.4±10.58				

Table 2: Time for onset of sensory block (min)

Study group	Onset time (min)	Mean difference	t* value	P value	Significance
B	19.1±1.7	8.7	23.05	P < 0.001	HS
BC	31.4±10.58				

* Student's unpaired t test HS – Highly significant

Table 3: Time for onset of motor block (min)

Study group	Onset time (min)	Mean difference	t* value	P value	Significance
B	15.46 ±2.25	6.53	14.63	<0.001	
BC	8.93±0.94				

Table 4: Duration of sensory block (hours)

Study group	Duration of block (hrs)	Mean difference	t* value	P value	Significance
B	5.81 ±0.59	8.11	34.49	<0.001	HS
BC	13.92 ±1.14				

Table 5: Duration of motor block (hours)

Study group	Duration of block (hrs)	Mean difference	t* value	P value	Significance
B	5.12 ±0.49	3.47	22.60	<0.001	HS
BC	8.59±0.67				

Table 6: Number of rescue analgesics in post-op 24 hours

No. of RA in 24 hours post-op	BUPIVACAINE	BUPIVACAINE + LONIDINE
1	0	24 (80)
2	21 (70)	6 (20)
3	9 (30)	0

Table – 7: Sedation score

Time of Assessment	Scores *	Bupivacaine	Bupivacaine Clonidine	X^2 Value, Significance
0 min	1	30 (100)	30 (100)	-
	2	0	0	No Difference
5 min	1	30 (100)	30 (100)	-
	2	0	0	No Difference
15 min	1	30 (100)	24(80)	P<0.05 Sig
	2	0	6 (20)	
30 min	1	30 (100)	21(70)	P<0.05 Sig
	2	0	9 (30)	
60 min	1	30 (100)	27 (90)	P<0.05 Sig
	2	0	3 (10)	
2 hrs	1	30 (100)	30 (100)	-
	2	0	0	No Difference
6 hrs	1	30 (100)	30 (100)	-
	2	0	0	No Difference
12 hrs	1	30 (100)	30 (100)	-
	2	0	0	No Difference
24 hrs	1	30 (100)	30 (100)	-
	2	0	0	No Difference

4.DISCUSSION

In our study we found that the onset of sensory and motor blocks was significantly faster in patients who received a combination of Clonidine and Bupivacaine. Onset of sensory block (group BC, 10.4 ± 1.1 min; group B, 19.1 ± 1.7 min). Onset of motor block (group BC, 8.93 ± 0.94 min; group B, 15.46 ± 2.25 min).

This could be due to a local direct action of Clonidine and its synergistic action with that of local anaesthetics. The onset of motor block was found to be faster than the onset of sensory block in both groups. Winnie et al.[4], observed this also, and attributed this to the somatotrophic arrangement of fibres in a nerve bundle at the level of the trunks in which motor fibres are located more peripherally than sensory fibres. Hence, a local anaesthetic injected perineurally will begin to block motor fibres before it arrives at the centrally located sensory fibres.

Our results showed that sensory block tended to last longer as compared to motor block which agrees with the observation by de Jong et al.[5] These authors explained that large fibres require a higher concentration of local anaesthetic than small fibres. The minimal effective concentration of local anaesthetic for large (motor) fibres is greater than for small (sensory) fibres. Thus, motor function return before pain perception and duration of motor block is shorter than the sensory block.

In our study duration of motor block was prolonged when clonidine was added to bupivacaine. (group BC, 8.59 ± 0.67 hrs; group B, 5.12 ± 0.49 hrs). In our study, the mean duration of sensory block (i.e. time elapsed from time of injection to appearance of pain requiring analgesia) was significantly higher (P <0.05) in group BC than in group B. (group BC, 13.92 ± 1.14 hrs ; group B, 5.81± 0.59 hrs).

In our study, the number of patients who required rescue analgesia and the mean number of supplemental analgesic boluses required were also significantly lower in patients in Group BC. Similar observation was made in the above mentioned study by Chakraborty et al.[6], The prolonged analgesia in Group BC could be due to the action of Clonidine by inhibiting action potential of A & C fibers in peripheral nerves as demonstrated by Gaumann et al.[7], Many authors favor the hypothesis that Clonidine exerts its local anesthetic-prolonging effect directly on nerve fiber, as a result of complex interaction between Clonidine and axonal ion channels or receptors.
Masuki et al.[8], suggested Clonidine may produce local vasoconstriction resulting in a delayed absorption of local anesthetic and block prolongation. Butterworth et al.[9],found Clonidine to produce tonic and phasic block of nerve conduction in rat sciaticnerve fibers by directly binding to Alpha-2 adrenergic receptors on presynaptic peripheral nerves to modify neuronal excitability.

We studied Clonidine at a dose of 1 µg/kg, as others have used the same dosage in peripheral nerve block without any significant adverse effects. Rashmi madan et al.[10], showed addition of 1 mcg/kg of clonidine to local anesthetic significantly prolonged duration of anesthesia after peribulbar block without side effects. Bernard et al.[11], evaluated effects of adding 30-300 mcg Clonidine to local anesthetic for brachial plexus block and found it is hemodynamically safe upto 150 mcg. A similar observations were made by Singelyn et al.[12], who suggested 0.5-1 mcg/kg of clonidine satisfactorily prolongs the analgesia of local anesthetic in peripheral nerve blocks without undue hemodynamic side effects of alpha-2 agonism.

In our study, sedation scores were higher in patients in Group BC compared to Group B, 15 min after injecting the drug until 60 min after injection. Similar observation was

made in the above mentioned study by Chakraborty et al.[6], This may have been due to partial vascular uptake of Clonidine, and its transport to the central nervous system where it acts and produces sedation. The limited duration of sedation could be explained by the fact that Clonidine is highly lipophilic and diffuses faster into the blood vessels. Though mean sedation score in group BC was higher as compared to group B ($P < 0.05$), we did not observe clinically significant sedation in patients in group BC. No patient experienced airway compromise or required airway assistance.

This mild sedation was actually desirable during that period. In conclusion, Clonidine 1 µg/kg when added to 25mL of Bupivacaine 0.5% for supraclavicular brachial plexus block, speeds the onset of sensory and motor blocks ($P < 0.05$). The combination produces improved analgesia, resulting in a prolonged effect and reduced requirements for rescue analgesics.

5.CONCLUSION

From our study, we conclude that, the addition of Clonidine (1µg / kg) as an adjuvant to bupivacaine (0.5%) has following effects :

i. Faster onset of sensory block.
ii. Faster onset of motor block.
iii. Longer duration of sensory block.
iv. Longer duration of motor block.
v. Less number of rescue analgesics in post-op 24 hours.
vi. Comfortable sedation intraoperatively without any need for airway assistance.
vii. No significant difference in haemodynamic variables i.e., pulse rate, systolic BP, diastolic BP and O2 saturation.

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