Effect of addition of clonidine to bupivacaine in supraclavicular block– a prospective randomised case control study

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Abstract

Background and Objectives: Supraclavicular block is one of the most common techniques of regional anaesthesia employed for upper limb surgeries. The practice of combining additives to local anaesthetics used in peripheral nerve blocks carries lot of advantages. Hence this study was designed to evaluate the effect of addition of Clonidine to Bupivacaine in Supraclavicular brachial plexus block.

Materials and Methods: We studied the addition of 100 µg of Clonidine to 0.375% bupivacaine compared with saline placebo in place of clonidine for nerve locator guided supraclavicular block using sublavian perivascular technique. Forty patients fulfilling inclusion criteria were divided into two groups, group B (Bupivacaine only group) and group BC (Bupivacaine and Clonidine group) and supraclavicular block was performed in them accordingly.

Results: The onset of motor and sensory blocks were quicker in group BC (4.25±0.72 min, 8.40±0.82 min respectively) compared to group B (6.40±1.14 min, 12.00±1.97 min respectively). The duration of motor and sensory block in group BC were longer (396.30±14.92 min, 466.75±13.91 min respectively) compared to group B (299.00±23.32 min, 328.95±34.13 min respectively). These were found to be statistically significant (p value < 0.05).

Conclusion: Adding clonidine to bupivacaine resulted in faster onset and longer duration of sensory and motor blockade. Intensity of postoperative analgesia also improved with mild intraoperative sedation and decreased heart rate without major haemodynamic instabilities.

Keywords: Supraclavicular brachial plexus, Clonidine, Bupivacaine, Nerve Locator and Upper limb surgeries.

Introduction

For surgeries on the upper limb, particularly in emergency situations, regional anaesthesia is more suitable than general anaesthesia. Supraclavicular block has been the most preferred choice among the available regional anaesthesia techniques.[1–3] The deposition of local anaesthetics in the supraclavicular region where the nerves of the brachial plexus are lying in close proximity results in a denser block with an early onset. Nerve locators help in identifying the plexus with reasonably good precision.[4] Additives to the local anaesthetic drugs have shown to offer various benefits like improvement in the duration of the nerve block.[5,6]

Aim

The aim of the study was to evaluate the effect of addition of 100µg of Clonidine to 0.375% Bupivacaine solution in Supraclavicular brachial plexus block performed for upper limb surgery.

Materials and Methods

The Study was conducted at Tertiary care Medical College Hospital in Tamilnadu. Approval of the institution ethical committee was obtained. A prospective randomized double blinded comparative study to evaluate, the effect of adding 100 µg of clonidine to 0.375% bupivacaine in nerve locator guided supraclavicular block by subclavian perivascular technique, was designed.

The study group included patients of either sex aged 20-60 years, weighing between 50-70 Kg belonging to ASA I and II categories posted for elective upper limb surgeries. Patients with known contraindications to the anaesthetic procedure and with known allergy to the drugs being used were excluded from the study.

Forty patients selected for the study were randomly allocated by slips in the box technique into groups B and BC. Informed written consent was taken from all patients; standard monitoring was done using electrocardiogram(ECG), noninvasive blood pressure(NIBP) and pulseoximetry(SpO2) throughout the study period. No sedative drugs were administered preoperatively to enable continuous neurological evaluation. Strict asepsis was maintained during the procedure.

Supraclavicular block was done by Subclavian Perivascular technique assisted by a peripheral nerve locator in both the groups. 30ml of 0.375% Bupivacaine with 2 ml of 0.9% sodium chloride was used for the block in group B, while patients in group BC received 30 ml of 0.375% bupivacaine with 100 µg of clonidine (1 ml of 150 µg was diluted with 2 ml of 0.9% NaCl solution. From this mixture 2 ml was mixed to the solution). The anesthetic solution was prepared by an anaesthetist not involved in the study. Both the patients and the operator performing the block were not aware of the drug solution being used. Inj.Diclofenac sodium

1.5 mg/Kg was given intramuscularly as a rescue analgesic in the postoperative period when the VAS score was more than 4.

The nerve plexus block was done using Braun Stimuplex DIG – Nerve locator and disposable Braun – Stimuplex insulated needle A 50 (22 G x 22"). Elbow flexion or finger flexion & extension of the hand were taken as the desired motor response during electrical nerve stimulation. In all the patients, once the desired motor response was obtained at 0.2-0.4 mA, 2-3 ml of the local anaesthetic mixture was injected in small increments with frequent testing for intravascular injection by intermittent aspiration. In case of selective sparing, the intercostobrachial and medial cutaneous nerve of the arm were blocked by infiltrating local anaesthetic subcutaneously.

After the procedure, sensory (using pin prick) and motor (assessment of muscle power) testing was done in all the patients and compared to the contralateral arm. Sensory testing was done along the distribution of Medial and Lateral cutaneous nerves of the arm, Medial, Lateral and Posterior cutaneous nerves of the forearm, Ulnar nerve, Median nerve and Radial nerve. Effect of motor block was assessed 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).

Hollmen's scale described below was employed to evaluate the sensory and motor block.[7]

Sensory block (Grade)
1. 0   – Pin prick felt normally
2. +   – Pin prick felt but weaker compared to contralateral extremity
3. ++   – Pin prick felt as blunt touch
4. +++ – Pin prick not felt

Grade 2 block was taken as the onset of block and grade 3 block was considered as complete block.

Motor block (Grade)
1. 0   – Normal muscle function
2. +   – Minimal depression in muscle function compared to pre-procedure status
3. ++   – Only very weak muscle action present
4. +++ – Absent muscle function

Grade 2 block was taken as the onset of block and grade 3 block was considered as complete block.

Sensory and motor evaluation was done every minute after the block was performed and the time of onset of the block was noted. The study group included only patient with complete sensory block and the rest were excluded. Time interval from the onset of sensory block to the onset of paraesthesia (during recovery) was taken as the duration of sensory block. Time interval between the onset and recovery of motor block was taken as the duration of motor block.

The five point sedation score given by Culebras et al[8,9] was employed to grade sedation
1. Alert and Awake
2. Sedated and responding to verbal commands
3. Sedated and responding to mild physical stimuli
4. Sedated and responding to moderate to severe physical stimuli
5. Not arousable

Heart rate, Blood pressure, Oxygen saturation and ECG were monitored throughout the surgery and postoperatively for 24 hours in all the patients. Pain assessment in the postoperative period was done using Visual Analog Scale with "0" representing "no pain" and "10" representing "worst possible pain". The observations were recorded for a period of 24 hours by the single investigator who was also blinded to the groups.

Statistical Analysis: Sample size was calculated taking duration of analgesia as the outcome measure of interest. To detect a difference of 30 minutes in this parameter between the two groups. It was estimated that 16 subjects would be required per group in order to detect a difference of 30 min in this parameter between the two groups, with 80% power and 5% probability of Type 1 error. This calculation assumed a pooled standard deviation of 30 min for the duration of analgesia. After dropout consideration, sample size of twenty patients per group was chosen.

Independent t – test was used to analyse data regarding age and weight of patients, onset, completion & duration of block. Chi-square test was employed to analyse intensity of block and sedation score. All the data were expressed as Mean$\pm$SD. P value of <0.05 was taken as statistically significant.

With regard to the haemodynamic parametes (Heart rate, Blood pressure etc.) a deviation of more than 30% of baseline was considered as a significant change.[8,10]

Results

Patients in both the groups were comparable with respect to the demographic profile. There was no significant difference in the mean duration of surgery between the two groups. (Table 1)

The mean time of onset and complete establishment of motor as well as sensory blocks in the Group BC, when compared to that in Group B were significantly less.(Fig. 1 & 2) Motor block got established earlier than sensory block in both the groups (p <0.05). The mean total duration of motor and sensory blocks in the Group BC when compared to that in Group B were significantly longer (Table 2 & Fig. 3). It was also found that the intensity of motor and sensory blocks were not statistically different between the two groups.(Table 3)
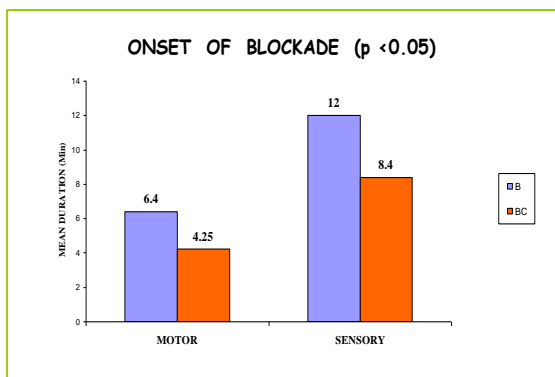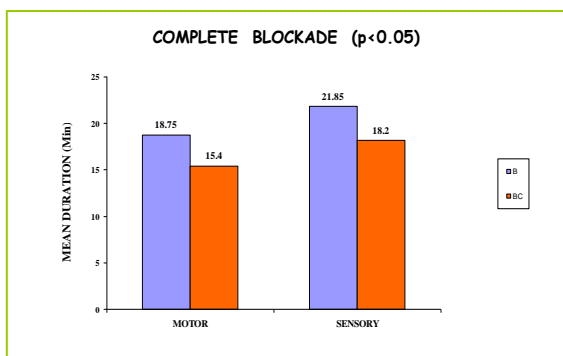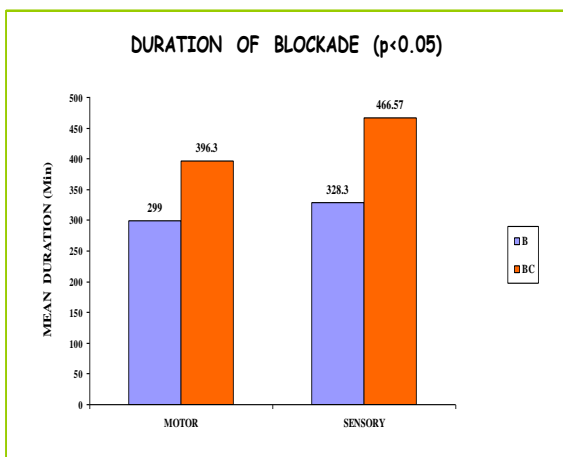
Fig. 1

Fig. 2

Fig. 3

Table 1: Mean duration of surgery

Groups	Mean duration of surgery (Minutes)	T	P Value
Group BC	94.00±12.83	0.65	0.517
Group B	91.00±16.03		

Table 2: Onset, completion & duration of block

Mean Time (Minutes)	Group BC	Group B	T	P Value
Onset of motor block	4.25 ± 0.72	6.40 ± 1.14	7.13	< 0.05
Onset of sensory	8.40 ±	12.00	7.53	< 0.001

block	0.82	± 1.97		
Complete motor block	15.40 ± 2.04	18.75 ± 2.71	4.42	< 0.05
Complete sensory block	18.20 ± 2.14	21.85 ± 2.37	5.11	< 0.05
Total duration of motor block	396.30 ± 14.92	299.00 ± 23.32	15.72	< 0.05
Total duration of sensory block	466.75 ± 13.91	328.95 ± 34.13	16.72	< 0.05

Table 3: Intensity of blockade

	Grading	Group B	Group BC
Motor	4	12(60%)	15(75%)
	3	5(25%)	4(20%)
	2	2(10%)	0
	1	0	1(5%)
Sensory	4	15(75%)	16(80%)
	3	5(25%)	4(20%)
	2	0	0
	1	0	0

During the intraoperative period (at 30 min), no patient in group B was sedated whereas in group BC, 50% were sedated requiring mild physical stimulus to awaken, 20% were sedated requiring verbal stimulus to awaken and the rest were not sedated. But even among the patients in Group BC who got sedated none required assistance in maintaining an open airway. Statistically significant difference ($X^2 = 21.53$; $p < 0.001$) was noted between both the groups with regard to sedation scores in the intraoperative period, but no such difference was noted with regard to sedation scores in the postoperative period. (Fig. 4)
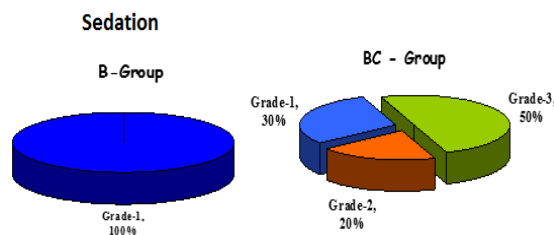

Fig. 4

Visual Analogue Scale was used to record pain in the patients postoperatively at 6, 12 and 24 hours. Lower mean VAS score was recorded in the patients in Group BC compared to those in Group B.(Fig. 5) Rescue analgesic requirement was also lower in patients in Group BC compared to those in Group B. Both these observations were found to be different on statistical testing.
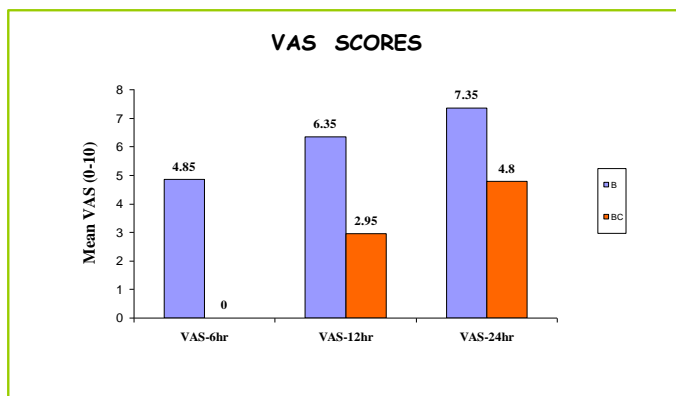
Fig. 5

In Group BC, heart rate decreased significantly during the intraoperative period compared to baseline values.(Fig. 6). Blood pressure values (Diastolic, Systolic and Mean Arterial Pressure) were lower in the Group BC compared to the control group, but this difference was not found to be statistically significant. No major haemodynamic instability (deviation of more than 30% over baseline values) prevailed in patient in both the groups during the study. (Table 4)
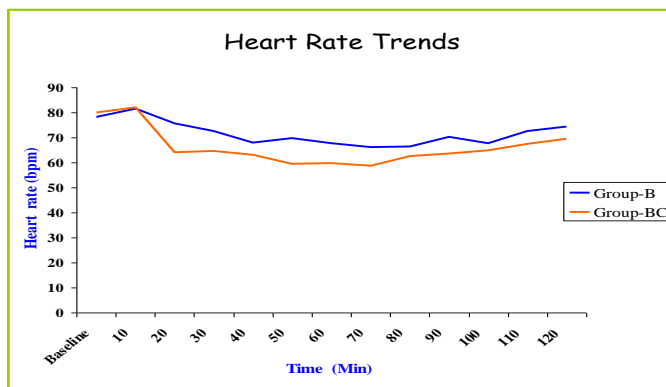
Fig. 6

Table 4: Vital parameters

Parameters	Group-B			Group-BC		
	Mean over 2hr	**Base Line**	**Deviation From baseline**	**Mean over 2hr**	**Base Line**	**Deviation From baseline**
Heart Rate bpm	71.01 (± 2.27)	78.10 (± 9.65)	-7.03 (± 8.54)	65.00 (± 2.29)	80.00 (± 7.71)	-15.00 (± 7.22)
Systolic BP mmHg	118.8 (± 4.06)	122.30 (± 9.10)	-3.5 (± 6.19)	113.74 (± 2.84)	119.05 (± 7.33)	-5.31 (± 6.80)
Diastolic BP mmHg	77.48 (± 2.68)	77.90 (± 5.75)	-0.42 (± 4.90)	75.03 (± 2.20)	79.75 (± 6.21)	-4.72 (± 4.97)
Mean Arterial Pressure mmHg	91.25 (± 2.88)	92.50 (±6.43)	-1.25 (± 4.78)	87.9 (± 2.47)	92.85 (± 6.13)	-4.95 (± 4.84)

During the study one incidence of accidental arterial puncture was noted in a patient in Group B. However no haematoma was noted, needle was repositioned and drug was administered. Block was successful. No other complications of supraclavicular block were noted during the study. One episode of bradycardia (Heart rate < 50/min) was noted in a patient in Group BC during the intraoperative period and was successfully managed with intravenous Inj.Atropine 0.6 mg.

Discussion

For surgeries on the upper limbs, brachial plexus block is an appropriate technique of anaesthesia. Various studies have explored the means of reducing complications with this technique.[1,11,12]

The previously commonly employed method of eliciting paraesthesia to confirm the proximity of the needle to the nerve plexus has long been an issue of debate. The possibility of neuronal damage caused by the blind advancement of the needle, the discomfort caused to the patient and the high failure rates have made this method less popular. Use of a nerve locator has been shown to aid in identifying the brachial plexus with good precision.[4,5,6,7,8] Though the use of ultrasound is gaining popularity, the high cost and lack of availability in the all operating areas precludes its widespread use in low resource settings.

Addition of adjuvant drugs like epinephrine,[5] opiods,[7] ketamine,[13] neostigmine[14] etc. to the local anaesthetic mixture for supraclavicular block has been shown to have many favourable effects like quickening the onset of block, increasing the duration of surgical anaesthesia, enhancement in the quality of block and decrease in the analgesic requirements in the postoperative period. But at times side effects have also been reported with the use of these additives.

Clonidine has been used as an additive to local anaesthetics in subarachnoid, epidural and caudal anaesthesia.[15–18] In a study by Bernard et al[19] the optimal clinical dose of clonidine as an additive has been shown as 60-100 μg. At this dose range, α2 agonistic side effects of clonidine have been found to be minimal. Based on this observation, in the present study a dose of 100 μg has been used. Clonidine has been shown to have additive action with that of local anaesthetics. The findings in the present study where the onset of sensory and motor blockade were quicker with addition of clonidine to local anaesthetics confirms this observation.

Winnie[20] has described the arrangement of sensory fibres in the centre and motor fibres in the periphery of a nerve trunk. This would explain the quicker onset of motor block than sensory block, which was observed in the present study.

De Jong et al[21] have shown that the minimal anaesthetic concentration of local anaesthetics for small (sensory) fibres is lesser than that for larger (motor) fibres. Parallel to this finding, in our study it was observed that the duration of sensory block was longer than motor block. During recovery from the block, perception of pain was delayed longer than the return of motor function. Pain scores in the postoperative period were lower in the patients in whom clonidine was used as an additive. Usage of rescue analgesic was also lower in the clonidine group.

The mechanism by which clonidine prolongs the action of local anaesthetics is not very clear. Clonidine has been shown to increase conduction of potassium in isolated neurons and block nerve conduction in Aγ and C fibres, thereby deepening the local anaesthetic induced conduction block. Few studies[22,23] have proven that peak plasma concentration of local anaesthetics are unaltered when clonidine is added. This finding supports the concept that clonidine produces its effects mainly by its pharmacodynamic properties. Other studies[24–26] have shown that clonidine decreases the peak plasma concentration of local anaesthetics. In a study by Sia et al,[27] clonidine by itself was found to be incapable of producing blockade of nerves. These observations suggest that clonidine produces its effects in the context of potentiation of nerve conduction block by its pharmokinetic properties.

Sedation produced by clonidine is a side effect. However, during the intraoperative period, the milder degrees of sedation produced by clonidine was found favourable. Moreover, there were no episodes of deeper levelsns of sedation causing airway compromise. Though haemodynamic instability was not observed in either of the groups, significant bradycardia was observed during the intraoperative period with the use of clonidine. Vascular uptake and action in the central nervous system[28] could explain these side effects of clonidine.

Conclusion

Clonidine in a dose of 100μg, as an additive to 0.375% Bupivacaine in Supraclavicular brachial plexus block, hastens the onset of sensory & motor blockade and prolongs the duration of sensory & motor blockade. Along with improvement in the quality of postoperative analgesia. Mild degrees of sedation and bradycardia without any major haemodynamic instability were also noted with this combination. Clonidine can thus be considered as a safe additive to local anaesthetic solution for brachial plexus blocks. Nerve locator is a safe and essential tool for performing supraclavicular brachial plexus block.

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