Original Research Article

Effect of bupivacaine and bupivacaine-clonidine combination in supraclavicular brachial plexus block – A comparative study

Prashant Sirohiya[1*], Kiwi Mantan[2], H. Rehman[3], Meera Kumari[2], Vishal Devra[4], Raghvendra Singh[1]

[1]Senior Registrar, [2]Assistant Professor, [3]Senior Professor, [4]Senior Resident
Department of Anesthesiology, Sardar Patel Medical College, Bikaner, Rajasthan, India
[*]Corresponding author email: **sirohiyaprashant@gmail.com**

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Abstract

Addition of clonidine to local anesthetics improves peripheral nerve blocks by reducing the onset time, improving the efficacy and extending postoperative analgesia. This study evaluated the effect of Bupivacaine clonidine combination in supraclavicular brachial plexus block for upper limb surgeries. A randomized double-blind controlled trial was performed in 60 patients. **Group B (n=30)** patients received 25 mL 0.5% Bupivacaine and 0.2 mL of Saline, whereas **group C (n = 30)** received 25 mL 0.5% bupivacaine and 0.2 mL (30 mcg) clonidine through supraclavicular brachial plexus block. In both groups, differences between age, sex, ASA grades, weight, vital parameters were statistically insignificant. Time of onset of sensory blockade and motor blockade were reduced in group C compared to Group B and were statistically significant. Duration of sensory and motor blockade were prolonged in group C compared to Group B and were statistically significant. Duration of post operative analgesia was prolonged in group C compared to Group B and were statistically significant. Sedation score of patients in group C were higher than those in group C intra-operatively and postoperatively. No clinically significant differences were observed in pulse rate, mean blood pressure and oxygen saturation. Due to its sedative properties, it can reduce patient anxiety and provide optimal intra-operative and postoperative patient comfort.

Key words

Supraclavicular, Bupivacaine, Clonidine, Analgesia.

Introduction

Peripheral nerve blocks have assumed a prominent role in modern anaesthesia practice as they provide ideal operative conditions without any sedation or systemic hemodynamic effects [1].

Brachial plexus block is commonly used regional anesthetic technique for surgeries involving upper limb. With advances in the field of surgery, surgical procedures have become more complex and the operating time has increased manifold with a consequent need to increase the duration of brachial plexus block [2]. Brachial plexus blocks provide a useful alternative to general anesthesia for upper limb surgeries. They achieve near ideal operating conditions by producing complete muscle relaxation, maintaining stable intra-operative hemodynamics and associated sympathetic block. The sympathetic block decreases post-operative pain, vasospasm and oedema [3].

Supraclavicular brachial plexus block is the preferred regional anaesthesia for upper limb surgeries. Here, the brachial plexus is presented most compactly at the proximal division or at the trunk level that provides most reliable anaesthesia for upper limb surgeries by anaesthetising the middle and lower plexus over 80% of the times (median, radial and ulnar) [4].

Certain drugs may be used as adjuvant to local anaesthetics to lower doses of each agent and enhance analgesic efficacy while reducing the incidence of adverse reactions. Tramadol and Fentanyl had been successfully used as adjuvants to local anaesthetics in brachial plexus block [5, 6]. The concurrent injection of α_2 adrenergic agonist drugs has been suggested to improve the nerve block characteristic of local anaesthetic solutions through either local vasoconstriction and facilitation of C fiber blockade [7] or a spinal action caused by slow retrograde axonal transport or simple diffusion along the nerve.

Clonidine is a selective α_2 adrenergic agonist with some α_1 adrenergic property. In clinical studies, the addition of clonidine to local anaesthetic solutions improved peripheral nerve blocks by reducing the onset time, improving the efficacy of the block during surgery and extending postoperative analgesia [8, 9]. The effect of clonidine is dose related between 0.1 and 0.5 μg/kg [9].

Clonidine possibly enhances or amplifies the sodium channel blockade action of local anaesthetics by opening up the potassium channels resulting in membrane hyperpolarization, a state in which the cell is unresponsive to excitatory input [10].

A number of these studies have focused on the effect of clonidine as adjuvant to either lignocaine [9] or mepivacaine [8]. Further, these studies were done using clonidine 150 μg, a moderately high dose with its attendant risk of adverse drug reactions. In a few clinical studies, a lower dose of clonidine (0.1-0.5 μg/kg) was used as adjuvant for brachial plexus block [9].

This study was comparing the effect of low dose clonidine versus placebo as adjuvant to bupivacaine for brachial plexus block, by supraclavicular approach, for surgical procedures of moderate duration.

The aim of this study was to evaluate whether additional anaesthetic and analgesic effects could be derived from administration of Clonidine, an α_2 adrenergic agonist, into brachial plexus block by supraclavicular approach.

Materials and methods

Study was conducted in Sardar Patel Medical College, Bikaner from June 2014 to July 2015

and was approved by Institutional Ethical Committee. A randomized double-blind controlled trial was done in 60 ASA I/II patients undergoing upper limb surgeries. Patients selected were of Age 18-60 years, ASA Grade I and II. Exclusion criteria were patients with a history of significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal, hepatic disease; alcoholism or drug abuse; pregnancy or lactating women; and patients receiving adrenoceptor agonist or antagonist therapy or chronic analgesic therapy. Also excluded were patients with morbid obesity, diabetes, peripheral vascular disease, suspected coagulopathy, or known allergies.

Details of the anaesthetic technique and the study protocol were fully explained to patients during pre-anesthetic check-up and informed written consent was obtained from each patient. Relevant investigations were performed as required. Patients, randomly allocated by computer generated randomisation list divided into two groups B and C.

Group B (n = 30) - 25 mL 0.5% Bupivacaine and 0.2 mL saline

Group C (n = 30) - 25 mL 0.5% bupivacaine and 0.2 mL (30 mcg) clonidine

On arrival in the operation room, baseline heart rate, blood pressure and oxygen saturation were recorded and monitored throughout the procedure. An intravenous line was secured in the unaffected limb and Ringer's lactate was started. Before the procedure, visual analogue scale (VAS) on 0-10 was explained to the patient for the assessment of pain where 0 denotes no pain and 10 denotes worst pain. All the patients received brachial plexus block through the supraclavicular approach.

The patient was placed in a semi-sitting position with the head rotated away from the site to be blocked and the shoulder pulled down. The arm rests comfortably on the side.

Main landmark is lateral insertion of the sternocleidomastoid muscle onto the clavicle and the clavicle itself. To facilitate the recognition of the sternocleidomastoid muscle, the patient was asked to elevate the head off the pillow. Once the sternocleidomastoid is identified, a mark was placed on the clavicle at its lateral insertion.

After painting the area with Povidone iodine and spirit, area was covered with sterile hole towel and then lateral insertion of the sternocleidomastoid muscle was identified on the clavicle, the plexus was located by palpation. When the plexus was found, the point of needle insertion was located immediately cephalad to the palpating finger. The nerve stimulator was connected to the stimulating needle and was set to deliver a 0.8 to 1.0 mA current at 1 Hz frequency and 0.1 ms of pulse duration. The needle was inserted first in an antero-posterior direction, almost perpendicular to the skin with a slight caudal orientation.

The needle was slowly advanced until the upper trunk is identified by a muscle twitch of the shoulder muscles. At this point, the orientation of the needle was changed to advance it caudally under the palpating finger, with a slight posterior angle. This strategy directs the needle from the vicinity of the upper trunk (shoulder twitch) to the front of the medial trunk (biceps, triceps, pectoralis twitch) on its way to the lower trunk (fingers twitch).

The goal of this block was to bring the tip of the needle in the proximity of the lower trunk, which was manifested by a twitch of the fingers in either flexion or extension.

Once the elicited motor response of the fingers was obtained at 0.5 mA, the injection is carried out after gentle aspiration. Injecting in the proximity of the lower trunk (motor response of the fingers) was the most important factor in accomplishing a successful supraclavicular brachial plexus block.

Sensory block (four nerve territories) was assessed by pin prick test using a 3-point scale: 0 = normal sensation, 1 = loss of sensation of pin

prick (analgesia), and 2 = loss of sensation of touch (anesthesia).

Motor block was determined by thumb abduction (radial nerve), thumb adduction (ulnar nerve), thumb opposition (median nerve), and flexion of elbow (musculocutaneous nerve) according to the modified Bromage scale [2] on a 3-point scale:

Grade 0: Normal motor function with full flexion and extension of elbow, wrist, and fingers

Grade 1: Decreased motor strength with ability to move the fingers only

Grade 2: Complete motor block with inability to move the fingers

Onset of motor blockade was considered when there was Grade 1 motor blockade. Peak motor block was considered when there was Grade 2 motor blockade.

Both sensory and motor blocks were assessed every 3 min till their onset and at 15, 30, 45, 60, 90, and 120 min; and then hourly (even after surgery) after the completion of injection, until they had resolved. Patients were asked to note the subjective recovery of sensation and movements which was then certified by an anesthesiologist or nurse.

Onset time for sensory block was defined as the time interval between the end of local anaesthetic administration and complete sensory block (score 2 for all nerves). Duration of sensory block was defined as the time interval between the complete sensory block and complete resolution of anaesthesia on all the nerves (score 0). Onset time for motor block was defined as the time interval between total local anaesthetic administration and complete motor block (grade 2). Duration of motor block was defined as the time interval from complete motor block to complete recovery of motor function of hand and forearm (grade 0).

Vitals were recorded at intervals of 5 min for first 30 min ,then after every 10 min till end of surgery ,and then hourly after surgery. Sedation score was assessed according to the modified Ramsay Sedation Scale (RSS) [11] from 1-6 as follows: 1 = anxious, agitated, restless; 2 = cooperative, oriented, tranquil; 3 = responds to commands only; 4 = brisk response to light glabellar tap or loud noise; 5 = sluggish response to light glabellar tap or loud noise; 6 = no response. Adverse effects comprised hypotension (i.e. 20% decrease relative to baseline), bradycardia (HR <50 beats/min), nausea, vomiting, and hypoxemia (SpO_2 <90%). Any need for additional medication was noted intra-operatively. Blood loss was calculated by the gravimetric method and replaced if more than the allowable blood loss. Pain was assessed using visual analogue scale (VAS) 0-10. Nursing staff was directed to administer inj. diclofenac sodium 3 mg/kg intramuscular when VAS $\geq$ 3 (rescue analgesia). The time between the complete sensory block and the first analgesic request was recorded as duration of post operative analgesia (DOPOA).

The data was compiled and subjected to statistical analysis using Statistical Package for Social Sciences (SPSS), version 16. Demographic and hemodynamic data were subjected to Student's *t*-test and for statistical analysis of onset time and duration of sensory and motor blocks, and Duration of post operative analgesia, unpaired *t*-test was applied. P-value < 0.05 was considered as statistically significant and $P < 0.001$ as highly significant.

Results

Supraclavicular brachial plexus block was performed in 66 patients, out of which six (four in group B and two in group C) were excluded due to incomplete block effect. A total of 60 patients (30 in each group) were included in the study. In both groups differences between age, sex, ASA grades, weight, vital parameters were statistically insignificant. (**Table - 1**)

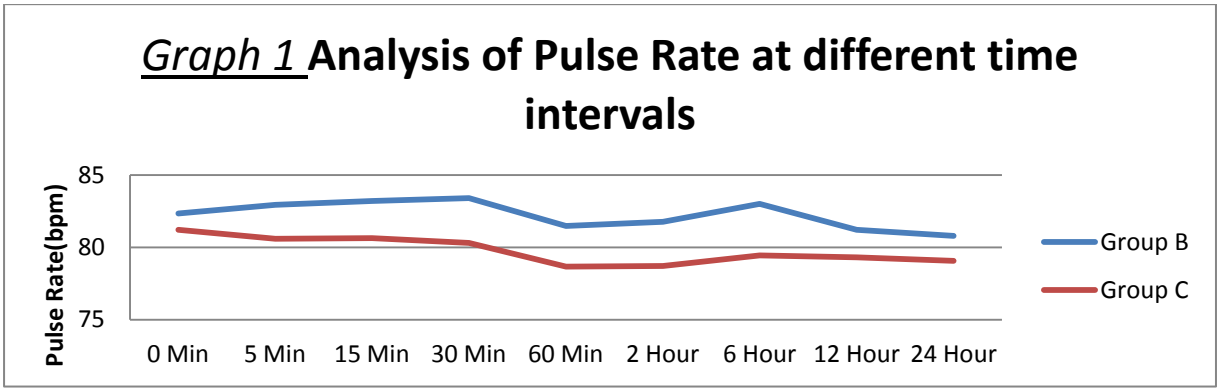
Time of onset of sensory blockade and motor blockade were reduced in group C compared to Group B and were statistically significant.

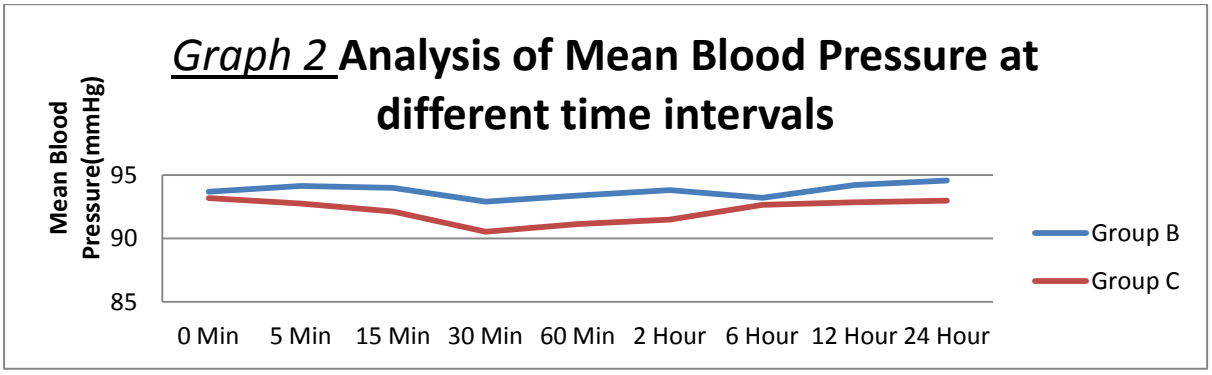
Duration of sensory blockade, motor blockade and post operative analgesia were prolonged in group C compared to Group B and were statistically significant. The modified RSS for group C was either 2/6 (in 21 patients) or 3/6 (in 9 patients), while that for group B was 1/6. (**Table - 2**)

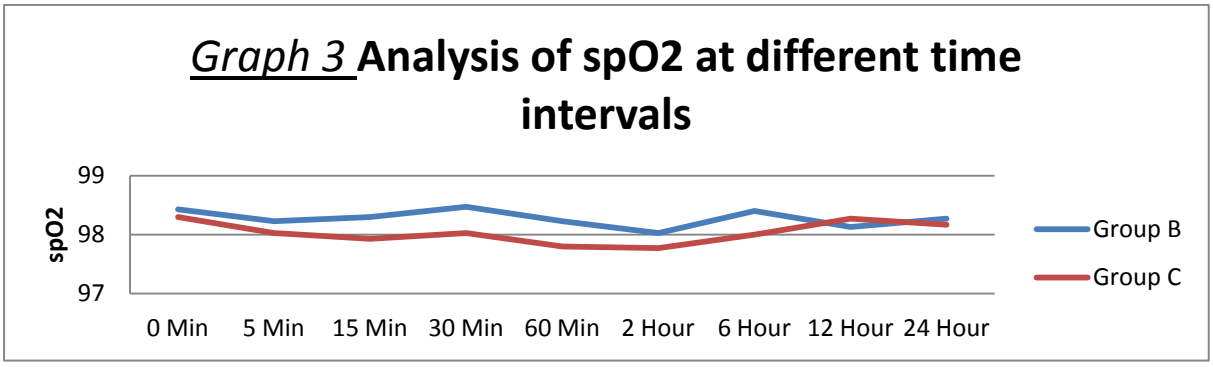
Table No.1 **Distribution According To Demographic Profile**			
	Group B	**Group C**	**P Value**
Age(Year)	31.10 +/- 14.23	32.73+/-11.71	0.629
Sex(M/F)	24/6	26/4	0.129
Weight(Kg)	71.03 +/-7.48	73.43 +/- 6.79	0.198
ASA Grade(I/II)	29/1	30/0	0.313

Table No.2 **Time profiles of sensory and motor blocks and duration of Post operative analgesia**			
	Group B	**Group C**	**P Value**
Time of onset of sensory blockade(min)	11.67 ± 4.13	4.90 ± 2.19	<0.001
Time of onset of motor blockade(min)	22.23 ± 8.83	6.03 ± 3.89	<0.001
Duration of sensory blockade(min)	280.5 ± 101.79	474.33±166.64	<0.001
Duration of motor blockade(min)	307.50 ± 103.21	515.3 ± 174.66	<0.001
Duration of post operative analgesia(min)	331.00 ± 98.04	550.17±182.50	<0.001

No clinically significant difference was observed in pulse rate, mean blood pressure and oxygen saturation (**Graph - 1, 2, 3**). No clinically significant adverse effects seen.







Discussion

A variety of receptors mediate anti-nociception on peripheral sensory axons. The peripheral administration of appropriate drugs (Adjuncts) may have analgesic benefit and reduce systemic adverse effects. In an attempt to improve perioperative analgesia, a variety of adjuncts such as opioids, verapamil, neostigmine and tramadol have been administered concomitantly with local anaesthetics into the brachial plexus sheath. The aim of this study was to evaluate whether additional anaesthetic and analgesic effects could be derived from administration of Alpha-2 adrenoceptor, Clonidine, into brachial plexus sheath.

The study was a prospective, randomized, double blind study conducted in Sixty ASA I and II patients undergoing elective upper limb surgery. Patients were divided into 2 groups of 30 each (group B and group C). Group B received supraclavicular brachial plexus block with 25 mL of 0.5% Bupivacaine and 0.2 mL of Saline and Group C received supraclavicular brachial plexus block with 25 mL of 0.5% Bupivacaine and 0.2 mL (30 μg) of Clonidine. Parameters observed include time of onset of sensory blockade, time of onset of motor blockade, duration of sensory blockade, duration of motor blockade and duration of postoperative analgesia.

Time of onset of sensory blockade was earlier in group C having a mean value of 4.90 min±2.19 min in comparison with control group having mean value of 11.67±4.13 min which is statistically significant ($p \leq 0.001$). This observation well matches with study of Chakraborty, et al. [12], time of onset of sensory blockade was 6.2 ± 0.78 min and 8.7 ± 1.01 min in Clonidine group and control group respectively. Iohom, et al. [13] noted that onset time of sensory block was faster in Clonidine group by 3.4 minutes compared to that of placebo. The meta-analysis conducted by Popping, et al. [14] on various studies using Clonidine in brachial plexus block also reinforce the fact that clonidine group has an early onset time of sensory block.

In our study, time of onset of sensory blockade was earlier in group C having a mean value of 4.90 min±2.19 min in comparison with control group having mean value of 11.67±4.13 min which is statistically significant ($p \leq 0.001$). This observation well matches with study of Chakraborty, et al. [12], time of onset of sensory blockade was 6.2 ± 0.78 min and 8.7 ± 1.01 min in Clonidine group and control group respectively. Iohom, et al. [13] noted that onset time of sensory block was faster in Clonidine group by 3.4 minutes compared to that of placebo. The meta-analysis conducted by Popping, et al. [14] on various studies using Clonidine in brachial plexus block also reinforce the fact that clonidine group has an early onset time of sensory block.

In our study, we observed that onset of motor block was earlier in group C having the mean value of 8.83 ± 3.89 min and in comparison, the group B had a mean value of 22.23 ± 6.03 min. which is statistically significant ($p = < 0.001$).

This observation matches well with the study conducted by Chakraborty, et al. [12], who had earlier onset of motor blockade in Clonidine group compared to control group, 10.6±1.36 min and 18.1±1.35 min respectively. However, Popping, et al. [14] had contrasting results in which clonidine had no significant impact on onset time of motor blockade.

The duration of sensory blockade in our study was 474.33 ± 166.64 min with Clonidine group and 280.50 ± 101.79 min for control group, which is statistically significant (p= <0.001). Iohom, et al. [13] in his study, found that the duration of sensory block was longer in Clonidine group by a difference of 112 min as compared with placebo, these observations were similar to our study. In a study conducted by Iskandar, et al. [15] the duration of sensory blockade was longer in the Clonidine group by 85 min compared to the control group. Cucchiaro, et al. [16] in his study found significant prolongation of duration of sensory block with Clonidine group as compared to control group. In contrast, Duma, et al. [17] showed that there was no added advantage in terms of duration of blockade between the clonidine and placebo group.

In our study, the duration of motor blockade was found to be 515.33±174.66 min in group C compared to group B 307.50±103.21 min and this difference was statistically significant (p=0.001). In the meta-analysis conducted by Popping, et al. [14], the average duration of motor block was 405 min (range, 122–728) in control group, clonidine significantly prolonged the duration of block to 546 min. According to study conducted by Erlacher, et al. [18], the duration of motor blockade in the clonidine group was prolonged in comparison to control group.

During our study we noticed a decrease in systolic, diastolic as well as mean arterial blood pressure but none of the patient had hypotension (defined by decrease in blood pressure by 20%) and all patients maintained the hemodynamic parameters well within the normal range, which is similar to study conducted by Culebras, et al. [19]. In our study we recorded decrease in pulse rate but none of the patient had clinical bradycardia (decrease in basal pulse rate by 20%) which is similar to study conducted by Culebras, et al. [19].

The mean time from onset of block to request of analgesia is taken as total duration of analgesia. It was 550.17±182.50 min in Clonidine group and 331.00±98.04 min in control group which is statistically significant p≤0.001. According to Bernard, et al. [9] in their study, Clonidine reduced the use of supplementary intravenous anaesthetic agents for surgery and produced dose-dependent prolongation of analgesia, it reached a mean 770 min (range, 190-1440 min) for the largest dose 300 µg. According to Murphy, et al. [20], Clonidine provided an analgesic effect that lasted as long as 492 min which is twice the duration of placebo 260 min. In Popping, et al. [14] study, the duration of postoperative analgesia for control group was 461 min where as Clonidine significantly increased the duration to 584 min. Eledjam, et al. [21] in their study with Clonidine using the dose of 150 µg and 40 mL Bupivacaine of 0.25 % reported that block produced with the addition of Clonidine was longer (994.2±34.2) compared to epinephrine as adjuvant (control group) 728.3±35.8.

In our study, sedation scores were higher in patients in Group C compared to Group B. Similar observation was made in the above mentioned study by Chakraborty, et al. [12], 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. Though, mean sedation score in group C was higher as compared to group B ($P < 0.05$), we did not observe clinically significant sedation in patients in group C. No patient experienced airway compromise or required airway assistance. This mild sedation was actually desirable during that period.

The limitations of our study were that the duration of block effect was overlapped with the natural sleep pattern of the patient. The tissue trauma related to the extent of surgery too has a contributory effect. Finally, small sample size in each group might have limited the true clinical significance of our comparison.

Conclusion

Addition of 0.2 mL Clonidine (30µg) as adjuvant to 25 mL bupivacaine (0.5%) has following effects:

- Faster onset of sensory block.
- Faster onset of motor block.
- Longer duration of sensory block.
- Longer duration of motor block.
- Longer duration of Post operative Analgesia.

No significant difference found in hemodynamic variables i.e., pulse rate, systolic BP, diastolic BP and oxygen saturation. No serious complications were observed. So, use of clonidine as adjuvant with bupivacaine for supraclavicular block is more effective and safe compared to bupivacaine alone.

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