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Comparision of Bupivacaine with and without Clonidine as for Supraclavicular Approach to Brachial Plexus Block

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Abstract

Introduction: The role of peripheral nerve blockade was expanded for management of post operative pain and chronic pain. Tramadol and fentanyl had been successfully used as adjuvant to local anaesthetic in brachial plexus block. Clonidine seems to provide analgesic benefit without major adverse effects. *Aim:* To evaluate whether additional anesthetic and analgesic effects could be derived from administration of Clonidine, an α 2- adrenergic agonist, into brachial plexus sheath. To compare the effects of Inj. Bupivacaine and Injection Bupivacaine with Clonidine as adjunct, used for Supraclavicular approach to brachial plexus block. *Materials and methods:* The study was a prospective, randomized, double-blind study. Sixty patients aged between 18 and 60 years of physical status ASA 1 and 2 undergoing upper limb surgeries lasting more than 30 minutes were included in the study. Patients were randomized into 2 groups of 30 each. All patients received brachial plexus block with 40 ml of 0.25% Bupivacaine. In addition, Bupivacaine+clonidine group received Clonidine at the dose of 2 µg/kg. *Results:* Onset of sensory blockade (time between injection and total loss of sensation to temperature) was faster in group C (22.33±4.1 min) compared to group B (27.17±3.64 min), which was statistically significant. Duration of sensory blockade (the time between injection and complete recovery from sensory disturbance) was also longer in Bupivacaine +clonidine group (524.00±83.91 minutes) compared to Bupivacaine group (339.00±57.44 minutes) and this difference was both clinically and statistically significant (p=0.001). Onset of motor blockade was faster in Bupivacaine +clonidine group (26.83±3.34 minutes) compared to Bupivacaine group (29.50±2.74 minutes).The duration of motor blockade was longer in Bupivacaine +clonidine group (524.00±83.91 minutes) compared to Bupivacaine group (339.00±57.44 min) and this difference was both clinically and statistically significant (p=0.001). Also, the time for demand of analgesics was significantly prolonged in group C (527.67±81.79 minutes) compared to group B (340.00±58.07 minutes) this difference was also statistically significant (p= <0.001). *Conclusion:* Addition of Clonidine to Bupivacaine solution for brachial plexus block can modify the action of local anaesthetic solution by its local action. There were no clinically significant side effects noticed. Hence, Clonidine can form an useful adjuvant for Bupivacaine when used for brachial plexus block.

Keywords: Bupivacaine; Clonidine; Brachial Plexus Block.

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Introduction

Peripheral nerve blockade is now a well-accepted concept for comprehensive anaesthetic care. From the operative suite, the role of peripheral nerve blockade was expanded for management of post operative pain and chronic pain. The recent emergence of pain management and the advantage of regional over general anaesthesia in case of emergent surgeries and the increasing importance

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of outpatient (ambulatory) surgery in anesthetic practice demand a subspecialty, peripheral nerve block. 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) [1].

After synthesis of Lignocaine Lofgrens systematic study of a whole range of compounds, so laying the foundation for all subsequent studies of local anaesthetic drugs. From these studies have come derivatives of Lignocaine such as Mepivacaine, Prilocaine, Bupivacaine and Etidocaine. Local anaesthetic administered as regional nerve blocks are utilized in providing post-operative pain relief in many surgical procedures by blocking signal traffic to the dorsal horn. Certain drugs may be used as adjuncts to local anaesthetics to lower the dose of each agent and enhance analgesic efficacy while reducing the incidence of adverse reactions. Tramadol and fentanyl had been successfully used as adjuvant to local anaesthetic in brachial plexus block.

Several studies have demonstrated analgesic effects of "Clonidine", an alpha agonist, in local, spinal and epidural anaesthesia when combined with local anaesthetic Bupivacaine. This observation that Clonidine has analgesic effects at spinal level has stimulated research to examine analgesic effects in the periphery. It has direct local action on the nerve itself and facilitation of local anaesthetic action. Also, Clonidine seems to provide analgesic benefit without major adverse effects.

Aim of Study

The aim of this study is to evaluate whether additional anesthetic and analgesic effects could be derived from administration of Clonidine, an α 2- adrenergic agonist, into brachial plexus sheath.

Methods and Materials:

Sixty patients aged between 18 and 60 years of physical status ASA 1 and 2 undergoing upper limb surgeries lasting more than 30 minutes were included in the study. The study was carried out at King George hospital attached to Andhra medical college Visakhapatnam. The patients mainly included those undergoing orthopaedic, plastic and reconstructive surgeries.

Inclusion Criteria

Patients between 18 and 60 years, under physical status ASA 1 and ASA 2 scheduled for upper limb surgeries were included after obtaining ethical clearance from the Institution and informed written consent from the patients.

Exclusion Criteria

Patients with cardiovascular diseases (Ischemic heartdisease, hypertension, valvular heart disease), neuromuscular diseases, thyroid diseases, diabetes mellitus, hepatic or renal failure, pregnant women are excluded from the study.

The patients were randomly allocated into two groups: Bupivacaine + Clonidine group (n=30) and Bupivacaine group (n=30) in a double-blind fashion. Supraclavicular brachial plexus block was performed after eliciting paraesthesia. All the patients were premedicated with Intravenous Injection Midazolam 2 mg, 15 minutes prior to block.

Bupivacaine + Clonidine group (n=30) received 40 ml diluted solution containing Bupivacaine 0.25% with 2 μg/kg body weight of Clonidine for brachial plexus block.

Bupivacaine group (n=30) received 40 ml of 0.25% of Bupivacaine for brachial plexus block.

All necessary equipments and drugs needed for administration of general anaesthesia and for emergency resuscitation were kept ready in order to manage failure of block or complications occurring during procedure.

Preoperative Preparation

The study protocol was approved by the hospital ethical committee. All patients were visited and evaluated thoroughly on the day prior to surgery. During the preanaesthetic evaluation a thorough evaluation of all the systems were undertaken. The anaesthetic procedure to be undertaken including development of paraesthesia was explained to the patients and an attempt was made to alleviate the anxiety of the patient. A written informed consent was obtained. Preanaesthetic preparation of patient included a period of overnight fasting. All patients received oral diazepam 10 mg night before surgery. A meticulous airway assessment was also carried out. Routine laboratory examinations were conducted including complete haemogram, urine analysis and blood sugar, ECG and chest X-ray were done in patients above 40 years.

Procedure

Intravenous access was obtained in the limb opposite to that undergoing surgery with 18 G cannula. ECG monitoring, Pulse oximeter, Noninvasive blood pressure were connected and monitored in all the patients. The patient was placed in supine position with the head turned away from the side to be blocked. The arm to be anesthetized should be adducted, and the hand should be extended along the side towards the ipsilateral knee as far as possible. Using classic technique approach, the midpoint of the clavicle was identified and marked.

The posterior border of the sternocleidomastoid was palpated easily when the patient raised the head slightly. Palpating the belly of the anterior scalene muscle and moving towards interscalene groove with the fingers, a mark was made at approximately 1.5 to 2.0 cm above the midpoint of the clavicle. By palpating the subclavian artery at this site, the landmark was confirmed.

After appropriate preparation and injection of local anaesthetic 2% xylocaine to raise a skin wheal, 22-gauge needle was inserted at the point of entry above the midpoint of clavicle in the backward-inward-downward direction (BID). With the direction of needle was towards the first rib, Paraesthesia in the forearm or hand was elicited sometimes before and sometimes after reaching the first rib. After negative aspiration for air or blood Bupivacaine+clonidine group received 40 ml of 0.25% Bupivacaine and Clonidine 2 µg/kg. Bupivacaine group received 40 ml of 0.25% Bupivacaine.

The following parameters were observed:

1. Onset time of sensory blockade
2. Onset time of motor blockade
3. Duration of sensory blockade
4. Duration of analgesia.
5. Duration of motor block

Ramsay Sedation Scale [5]

1. Anxious, agitated or restless, or both
2. Cooperative, oriented, and tranquil
3. Responds to commands only
4. Brisk response to a light glabellar (forehead) tap or auditory stimulus
5. Sluggish response to a light glabellar (forehead) tap or loud auditory stimulus
6. No response

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Mann Whitney U test has been used to find the significance between two groups for parameters on non-interval scale.

Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

In the present study we analyzed statistical significance of the difference between group B (control) and group C (Clonidine). A `p` value of >0.05 meant that the difference between the groups was insignificant. A `p` value of < 0.05 was taken to be statistically significant and a value <0.01 was highly significant.

Results

Age group 21-30 are maximum in either group. Bupivacaine + clonidine group (11). Bupivacaine group (12). The average age was 35.33±10.85 years in Bupivacaine + clonidine group and 34.03±9.83 years in Bupivacaine group.

Sixty patients of either sex had participated in the study. Both groups had predominantly male patients.

The height in Bupivacaine with a mean of 156.77±4.21. Bupivacaine+clonidine group with a mean of 58.67±7.79. The maximum weight is 110 kg and a minimum of 48 kg in Bupivacaine group with a mean of 59.30±10.67 (Table 1).

Onset of blockade was group(22.33 +/-4.1 minutes) compared to Bupivacaine group (27.17+/-3.64 minutes): this difference was statistically significant (p=0.001) (Fig. 1).

It is faster in bupivacaine+clonidine group (26.83±3.34 minutes) when compared to bupivacaine group (29.50±2.74 minutes). It is statistically significant with P value <0.001 (Fig. 2).

The duration of sensory blockade in the two groups. Duration of blockade was longer in Bupivacaine + clonidine group (524.00±83.91 minutes) compared to Bupivacaine group (339.00±57.44 minutes) and this difference was statistically significant (p=0.001).

Table 1: Demographic distribution in study

Age in years	Bupivacaine+Clonidine Group		Bupivacaine Group	
	No	%	No	%
18-20	2	6.7	2	6.7
21-30	11	36.7	12	40.0
31-40	6	20.0	6	20.0
41-50	9	30.0	9	30.0
51-60	2	6.7	1	3.3
Total	30	100.0	30	100.0
Mean±SD				
Age in year	35.33±10.85		34.03±9.83	
Height in cm	158.73±6.37		156.77±4.21	
Weight in kilogram	58.67±7.79		59.30±10.67	
Gender				
Male	24	80.0	20	66.7
Female	6	20.0	10	33.3
Total	30	100.0	30	100.0

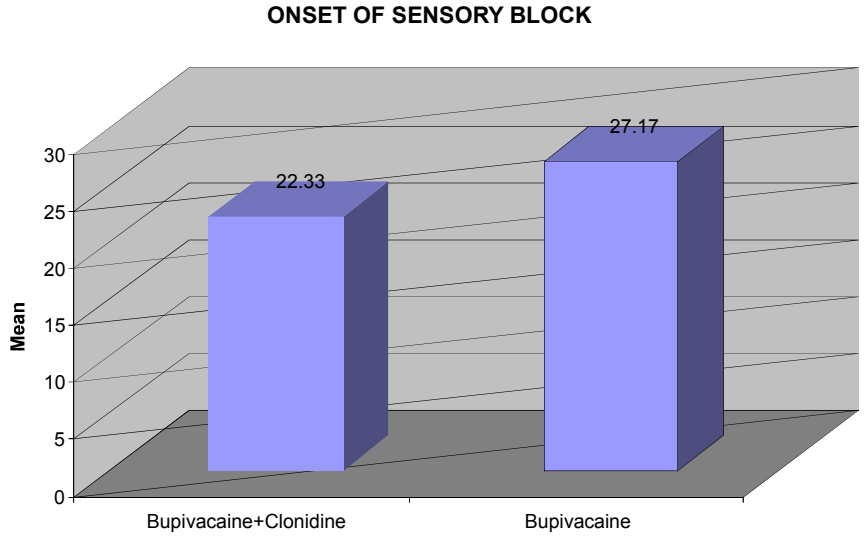

Fig. 1: Onset of sensory block

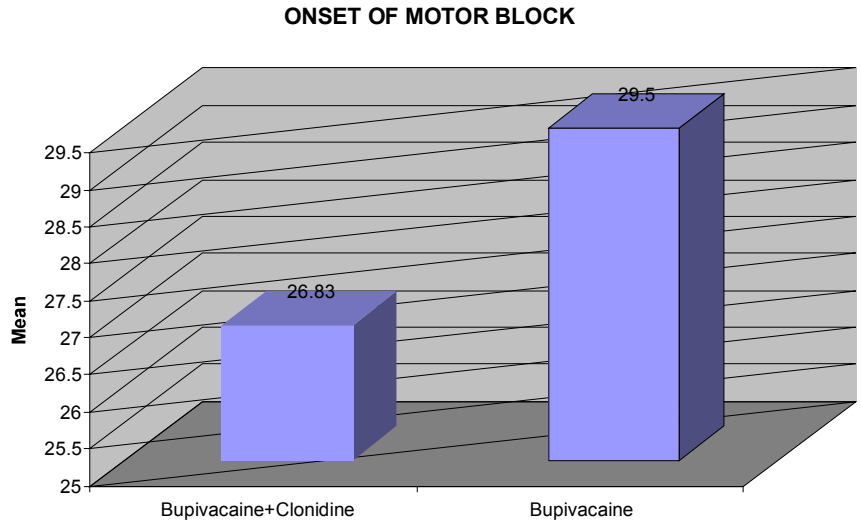

Fig. 2: Onset of motor block

Table 2: Duration of sensory block and analgesia

Duration of sensory block (minutes)	Bupivacaine+ clonidinegroup	Bupivacaine group	p value	Remark
	Mean	Mean	<0.001	Significant
	540.00±83.91	339.00±57.44		
	Duration of Analgesia (minutes)			
	527.67±81.79	340.00±58.07	<0.001	Significant
	Duration of Motor Block (minutes)			
	557.00±128.72	367.0±65.29	<0.001	significant

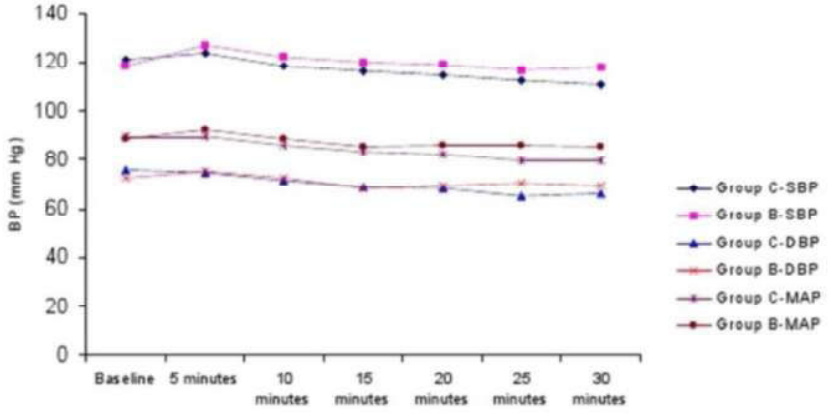

Fig. 3: Comparison of MAP (mm hg) between two groups of patients

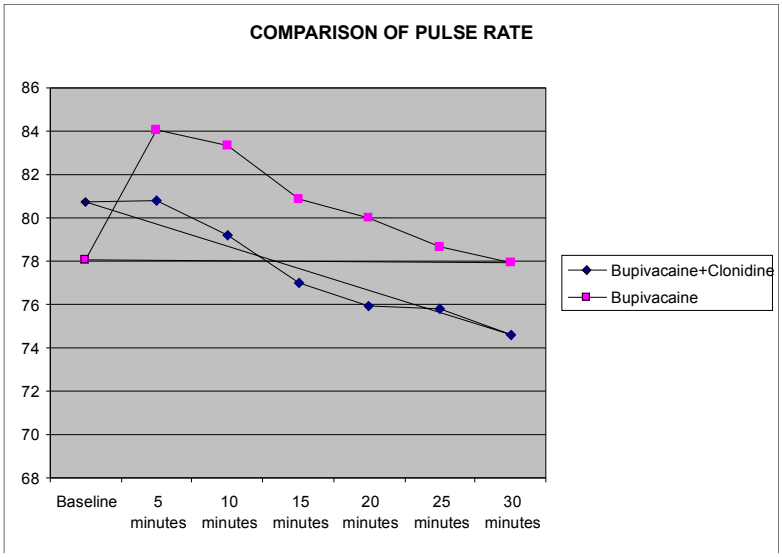

Fig. 4: Comparison of pulse rate between two groups of patients

Duration of analgesia was longer in Bupivacaine+clonidine group (527.67±81.79 minutes) compared to Bupivacaine group (340.00±58.07 minutes): this difference was clinically and statistically significant (p= <0.001).

Duration of motor blockade was longer in Bupivacaine+clonidine group (557.00±128.72 minutes) compared to Bupivacaine group (367.0±65.29 minutes) and this difference was statistically significant (p=0.001) (Table 2).

In the present study it is noticed that 10 mm of Hg mean decrease in systolic blood pressure and 9 mm Hg decrease in diastolic blood pressure in Clonidine group compared to control at 25th minute after performing brachial plexus block which is clinically and statistically not significant. Also we observed 10 mm of Hg mean decrease in Mean blood pressure in Clonidine group compared to control at 30th minute after performing brachial plexus block which is clinically and statistically not significant (Fig. 3).

Although we clinically noticed decrease pulse rate in Clonidine group by mean value of 6 beats per minute but this is not statistically significant (Fig. 4).

In our study, we found mean of 99% of saturation in both the groups this clinically and statistically not significant.

In the present study there are no observed any side effects in both the groups.

In the present study there is no undue sedation in either of groups and Ramsay Sedation score was 2 in both the groups.

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 anesthetics into the brachial plexus sheath. The aim of this study was to evaluate whether additional anesthetic and analgesic effects could be derived from administration of Alpha-2 adrenoceptor agonist, Clonidine, into brachial plexus sheath.

The study was a prospective, randomized, double-blind study carried out at king George hospital, Visakhapatnam Sixty ASA I and II patients undergoing elective upper limb surgery lasting more than 30 minutes were included in the study. Patients were divided into 2 groups of 30 each (Bupivacaine + clonidine group & Bupivacaine group). Group C received brachial plexus block with 40 ml of 0.25% Bupivacaine and 2 μg /kg body weight Clonidine. Group B received brachial plexus block with 40 ml of 0.25% Bupivacaine. Parameters observed include onset of sensory blockade, onset of motor block, duration of sensory blockade, duration of motor blockade and duration of analgesia.

Onset of sensory block

In the present study, it is observed that onset of sensory onset was earlier in study group of Clonidine having a mean value of 22.33±4.1 min in comparison with control group having mean value of 27.17±3.64 min, which is statistically significant (p = < 0.001).

This observation well matches with study of Susmitha chakraborthy [3], onset of sensory 6.2± 0.78 minutes and 8.7±1.01 minutes in Clonidine group and control group respectively. Very short duration of onset with this study may be because of higher concentration of Bupivacaine. Similar observation was made by Gabriella Iohom [4], where the onset time of sensory block was much faster in Clonidine group, 21.3±7.2 minutes compared to that of placebo (24.7±5.5 min). A Meta-analysis was conducted by Daniel M. Popping [2] on various studies using Clonidine doses ranging from 90 to 150 μg in Brachial plexus block. He found early onset of sensory block time with an onset time of Clonidine was 12.8 minutes. In controls, average onset of time of sensory block was 15 minutes.

Onset of motor block

In the present study, it is observed that onset of motor block was earlier in study group of Clonidine having the mean value of 26.83±3.34 minutes and in comparison, the control group had a mean value of 29.50±2.74 minutes. which is statistically significant (p = < 0.001)

This observation matches well with the study conducted by Susmitha Chakraborthy [3], who had earlier onset of motor blockade in Clonidine group compared to control group, 10.6±1.36 minutes and 18.1±1.35 minutes respectively. However, Daniel M. Popping [5] had contrasting result as time for onset of motor block, quantified by using the Bromage scale. In control group mean onset time of motor block was 18.3 minutes and Clonidine had no significant impact on onset time.

Duration of sensory block

The duration of sensory blockade, in the present study was 524.00±83.91 minutes with Clonidine group and 339.00±57.44 minutes for control group, which is statistically significant (p= <0.001).

Gabriella Iohom [4] in his study, found that the duration of sensory block was longer in Clonidine group compared with placebo 275±75 versus 163±57; p = 0.04, these observation were similar to the present study. In a study conducted by Henri Iskandar [6] the median sensory block was 235 min (195–250) in the Clonidine group, compared with 150 minutes (135–160) in the control group. Giovanni Cucchiaro [7] et al. in his study on children using 0.25% Bupivacaine found significant prolongation of duration of sensory block with Clonidine group 1140 min compared to control 840 min.

Duration of analgesia

The mean time from onset of block to request of analgesia is taken as total duration of analgesia. It was 527.67±81.79 in Clonidine group and 340.00±58.07 in control group which is statistically significant p = < 0.001. According to Bernard et al. [8] 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 300µ which matches well with our study. According to Murphy et al., Clonidine provided an analgesic effect that lasted as long as 492 minutes which is twice the duration of placebo group 260 minutes. In Daniel M. Popping [5] study, the duration of postoperative analgesia for control group was 461 minutes where as Clonidine significantly increased the duration 584 minutes. The present study observations concurrent with study conducted by Eledjam et al. [9] in supraclavicular block with Clonidine using the dose of 150 µg and 40 ml Bupivacaine of 0.25%. The block produced with the addition of Clonidine was longer (994.2±34.2) compared to epinephrine as adjuvant (control group) 728.3±35.8.

Duration of motor block

In this present study, the duration of motor blockade was found to be 557.00±128.72 minutes in Bupivacaine + clonidine group compared to Bupivacaine group 367.0±65.29 minutes and this difference was statistically significant (p=0.001).

In the meta-analysis conducted by Daniel M. Popping [5], the average duration of motor block was 405 minutes (range, 122–728) in control group. Clonidine significantly prolonged the duration of block to 546 minutes. According to study conducted by Wolfgang Erlacher et al. [10], the duration of blockade in the Bupivacaine group was 728 minutes in control, and in comparison the duration of motor blockade in Clonidine group is 972 minutes, which are matching well with the present study.

During the present study it was noticed systolic, diastolic as well as mean arterial blood pressure were decreased but none of the patient had hypotension (defined by decrease in blood pressure by 20%). and maintained the hemodynamic parameters well within the normal range, which is similar to study conducted by Eisenach JC et al. [11] and Culebras X et al. [12]. In the present study pulse rate decreased by 6 beats but none of the patient had clinical bradycardia (decrease in basal pulse rate by 20%). which is similar to study conducted by Eisenach JC [11] et al. and Culebras X et al. [12], Also in the present study no notice was made undue sedation in either of groups and Ramsay Sedation score [5] was 2 in both the groups.

Conclusion

Clonidine is an alpha-2 agonist known to prolong the analgesic actions of local anaesthetics by acting on peripheral nerve. We studied the anaesthetic and analgesic effects of adding Clonidine into brachial plexus sheath with Bupivacaine solution in 60 patients undergoing upper extremity orthopaedic, plastic or reconstructive surgery. Patients were randomized into 2 groups of 30 each. All patients received brachial plexus block with 40 ml of 0.25% Bupivacaine. In addition, Bupivacaine + clonidine group received Clonidine at the dose of 2 µg/kg.

In conclusion, addition of Clonidine to Bupivacaine solution for brachial plexus block can modify the action of local anaesthetic solution by its local action. The dosage 2 µ/kg body weight used in the study significantly increased the duration of analgesia and muscle relaxation. There were no clinically significant side effects noticed. Hence it is concluded that Clonidine can form an useful adjuvant for Bupivacaine when used for brachial plexus block.

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