

ORIGINAL ARTICLE:

A randomized double-blind controlled study to determine effect of clonidine as an adjuvant to bupivacaine in supraclavicular brachial plexus block at Jaipur, Rajasthan

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Abstract

Background: Clonidine, a selective alpha 2 adrenergic agonist, has been used traditionally as an anti- hypertensive agent, also used as an adjunct to local anaesthetic in peripheral nerve blocks. Present study was done to determine the effect of clonidine (2 mcg / kg) added to bupivacaine (0.5%) on onset and duration of analgesia and motor block in supraclavicular brachial plexus block .We also evaluated the side effects like hypotension, bradycardia, and sedation.

Methodology: This randomized double-blind controlled study included 60 ASA grade I and II patients (age 20-50years) undergoing elective surgery in upper limb. Group 1 (n=30) received 28 ml of 0.5% bupivacaine and 2 ml normal saline while Group 2 (n=30) received 28 ml of 0.5% bupivacaine and inj. Clonidine Hydrochloride 2 mcg/kg through supraclavicular approach for brachial plexus block. Vital parameters (Heart rate and non-invasive blood pressure) and sedation score were measured every 5 minutes till the end of procedure. Postoperatively heart rate, noninvasive blood pressure, pain score and sedation scores were recorded every 30 min till 2 hours and thereafter at 6 hours,12 hours and 24 hours. The onset and duration of sensory and motor block as well as duration of analgesia were recorded.

Results: The mean duration of analgesia in group 1 was 466.87 ± 75.02 (min) and group 2 was 876.80 ± 221.52 (min). (p value came out to be < 0.001) showing significant prolongation of duration of analgesia by adding clonidine. Moreover Group 1 experienced the mean severity of pain at first analgesic requirement more than group 2 and it was found to be statistically significant. No clinically significant difference in vital parameters and sedation score was noted.

Conclusion: Clonidine at the dose of 2 mcg / kg body weight added to 0.5% bupivacaine in supraclavicular brachial plexus block in upper limb surgeries is highly effective in prolongation of sensory analgesia and provides a better post operative period for the patient free of pain without any potential side effects.

Keywords : Clonidine, Adjuvant, Supraclavicular brachial plexus block

INTRODUCTION

Peripheral nerve block remains a well accepted component of comprehensive anesthetic care since Halsted first reported the use of cocaine to block upper extremity nerve in 1885.¹ Brachial plexus block with supraclavicular approach is used as an alternative or adjunct to general anesthesia for surgery of hand and arm. This was introduced into clinical practice in Germany by Kulenkampff.² Colloquially known as the “spinal of the arm” supraclavicular

block is advantageous as the brachial plexus nerves are tightly packed in this approach and rapid onset times as well as high success rate is often rapidly achieved.

Various studies have investigated several adjuncts to local anesthetics to improve the quality of onset and duration of block and decrease postoperative analgesic requirements and systemic effect like midazolam,³ adrenaline,⁴ hyaluronidase,⁴ magnesium sulphate,⁵ ketamine,⁵ dexamethasone,⁶ neostigmine⁷ and various Opioids⁸.

Clonidine, a selective alpha 2 adrenergic agonist, has been used traditionally as an anti hypertensive agent. Various studies have shown that clonidine can be used as adjunct to local anesthetics in peripheral nerve blocks. The proposed mechanism of action of clonidine as adjunct to local anesthesia are, centrally mediated analgesia, alpha 2 adrenergic receptor mediated vasoconstriction, attenuation of inflammatory response and direct action on peripheral nerves.⁹ Present study was done to determine the effect of clonidine 2 mcg / kg added to bupivacaine 0.5% on onset and duration of analgesia and motor block and also to evaluate the side effects such as hypotension, bradycardia, sedation in supraclavicular brachial plexus block.

OBJECTIVES

To determine the effect of clonidine 2 mcg / kg added to bupivacaine 0.5% in supraclavicular brachial plexus block on

1. Onset and duration of analgesia
2. Onset and duration of Motor block
3. Occurrence of side effects such as hypotension, bradycardia and sedation

MATERIAL AND METHODS

The study was conducted in the Department of Anesthesia, S.M.S Medical College, Jaipur. This double-blinded controlled study included 60 ASA grade I and II patients (age 20-50years) scheduled for elective orthopedic surgery in upper limb under supraclavicular brachial plexus block after approval from institutional ethical committee. Patients not willing to participate in the study, uncooperative patients, with pre existing respiratory, cardiac, hepatic or renal disorders, allergy to the drug used, bleeding disorder, severe neurological deficit or other contraindications to regional anesthesia were excluded from the study. Pre anesthetic checkup was done a day before the surgery and written informed consent was obtained for performance of block after complete explanation about the study protocol and the procedure. Patients were randomly divided into two groups of each of 30 patients by a computer generated random number list. Group 1 (n=30) received 28ml of 0.5% bupivacaine and normal saline while Group 2 (n=30) received 28ml of 0.5% bupivacaine and inj. Clonidine 2 mcg/kg. All the solutions were diluted with normal saline to make a total volume of 30 ml. The solutions were prepared by an anesthesia resident not involved in study. Once the patients arrived in operation theatre, standard monitors applied and intravenous access secured. Patients did not receive any premedication.

The patient was placed in the supine position, with the head turned away and the ipsilateral arm adducted. The interscalene groove and mid-point of the clavicle and subclavian artery were identified. After aseptic preparation of the area, at a point 1.5 to 2.0 cm posterior to midpoint of the clavicle a skin wheal was raised with a local anaesthetic (lignocaine 2% plain). Next, a 22G, 50 mm "short beveled" needle was passed through the same point in a caudal, slightly medial and posterior direction, until either a paresthesia is elicited or the first rib is encountered. If the first

rib was encountered, the needle was moved over the first rib until a paresthesia was elicited either in the hand or arm. After eliciting paresthesia and negative aspiration of blood, the study medication was injected (classic landmark technique).

After performance of nerve block patients were assessed for onset of sensory block every 1 minute by pin prick with 25 gauge needle. Assessment was done in all the dermatomal areas corresponding to all four nerves (radial, median, ulnar and musculo-cutaneous nerve). Sensory block was graded as-Grade 0- Sharp pain, Grade 1 - Touch sensation only, Grade 2 -Not even touch sensation

Motor block was assessed by modified Bromage scale every one minute. Brachial plexus block was considered successful by Vester-Andersen's criteria¹⁰ Vester Anderson's criteria.[7] i.e., complete when there is Sensory block in the entire distribution of arm except axillary nerve and incomplete when nil or incomplete sensory block in some of these nerves, or failed block when there is absence of sensory block in all major nerves or presence of sensory block in only one of the nerves.

Heart rate, non-invasive blood pressure, SPO2 & sedation score were measured every 5 minutes till the end of procedure. Postoperatively heart rate, noninvasive blood pressure, pain and sedation scores were recorded every 30 min till 2 hours and thereafter at 6 hrs, 12 hrs and 24hrs. Pain was assessed by numeric rating scale while Sedation was assessed by using Ramsay sedation score. The comparison between the two groups with respect to demographic variables, Intraoperative Vital parameters, onset and duration of sensory and motor blocks were compared between two groups using z-test. P value < 0.05 was considered significant. Epi Info software (CDC WHO) was used for all statistical analysis.

RESULTS

We recruited 30 patients each group and there was no drop outs. The age, sex distribution, body weight and duration of surgery was found to be comparable in both the groups (Table 1) Onset and duration of sensory and motor blocks have been presented in Table 2.

Table 1: Comparison of demographic and other relevant parameters at baseline between both the groups

	GROUP 1	GROUP 2	p value
Age(yrs) (mean±SD)	33.53 ± 7.49	34.37 ± 7.80	0.6745
Body wt(kgs) (mean±SD)	59.83 ± 4.98	59.97 ± 5.30	0.9204
Duration of surgery (min) (mean ± SD)	52.5 ± 9.72	51.83 ± 10.54	0.7999

Table 2: Onset and duration of analgesia and motor block minutes {mean + SD }

Time (minutes)	Group 1	Group2	P value	Significance
Onset of sensory block	12.43 ± 4.37	12.77 ± 4.22	0.7649	NS
Duration of analgesia	466.87± 75.02	876.80 ± 221.52	0.000	HS
Onset of motor block	16.1 ± 4.67	14.8± 4.65	0.2725	NS
Duration of motor block	426 ± 72.26	830.10 ± 214.48	0.000	HS

Table 3: Pain score

	Group 1	Group 2	P value	Significance
Severity of pain at first analgesic requirement	6.6 ± 1.04	4.97 ± 0.89	0.0000	HS

Table 4: Degree of sedation

S. No.	Degree of sedation	Group 1	Group 2
1	Awake and alert	30 (100%)	25 (83.33%)
2	Drowsy but responsive to command	0	5 (16.67%)
3	Very drowsy but responsive to pain	0	0
4	Unresponsive	0	0

Table 4 shows the degree of sedation. In group 1 all patients were awake and alert. In group 2 five out of thirty showed mild sedation. There was no statistically significant difference observed in heart rate, blood pressure, respiratory rate and oxygen saturation between two groups.

DISCUSSION

Brachial plexus block serves as sole anesthetic technique to facilitate painless surgery. It provides an excellent alternative for patients who are at high risk for general anesthesia. Various approaches have been described of which the classical supraclavicular approach is most suited for the whole of upper limb surgeries as it blocks all the branches of brachial plexus block. Longer acting local anesthetics have been used for brachial plexus block. Various studies have investigated several adjuncts that prolong the duration of analgesia.

Clonidine has been used as antihypertensive agent and as adjunct in intrathecal and epidural route. But the mechanism of action in peripheral nerve blocks is highly unclear. Clonidine blocks conduction of A- delta and C

fibres with some preference for C fibres and intensifies the conduction of local anesthetics. Clonidine seems to exert a local action at the peripheral nerve because subcutaneous or intra muscular injection of clonidine did not increase the duration of block.¹²

In the present study the effects of clonidine 2 mcg/kg added to 0.5% bupivacaine in supraclavicular brachial plexus block has been studied in terms of onset and duration of sensory analgesia and motor block and side effects. Sixty patients were given supraclavicular brachial plexus block. The patients were divided into 30 each: GROUP 1 (control group): 28 ml of 0.5% bupivacaine with 2 ml normal saline. GROUP 2 (Clonidine group): 28 ml of 0.5% bupivacaine with 2mcg / kg clonidine and normal saline to make a total volume of 30 ml.

Casati A et al evaluated the effects of 1 mcg/ kg body weight clonidine added to 20 ml ropivacaine 0.75% and found significant prolongation in post operative analgesia. B.M.¹³. Bernard et al observed small doses of clonidine 30 – 90 mcg in combination with lidocaine reduced onset time and prolonged duration of analgesia while 300 mcg were associated with significant adverse effects.¹⁴

In the present study clonidine 2 mcg/ kg body weight was used and significant results were found in prolongation of sensory analgesia. Among 30 patients who received clonidine the minimum dose was 104 mcg (52 kg) and maximum dose was 140 mcg (70 kg).

Lund et al reported the analgesia and anesthesia characteristics of bupivacaine in brachial plexus block complete analgesia occurred in 8 to 18 min(average 11 min) and return of normal sensation occurred in 6 to 15 hrs. (average 10 hrs).¹⁵ Dejong et al showed that the sequence of events after the performance of block was quite predictable he found that analgesia occurs first in the upper arm, then spreads towards the fingers until the arm is numb. While the analgesia front sweeps down the limb, weakness of the muscles of the upper arm begins to appear, becoming more pronounced till motor block ensues. During induction, sensory blockade persist long after motor function has recovered.¹⁶

In present study, the onset of sensory block and motor block in control group was 12.43 ± 4.37 and 16.1 ± 4.67 respectively. In clonidine group, sensory onset was 12.77 ± 4.22 and motor onset was 14.8 ± 4.65 . There was no significant difference in onset time. ($p > 0.05$). These results are consistent with the studies of Duma A et al¹⁷ where clonidine was used as adjunct to bupivacaine. Duma A et al concluded from their study that the onset time for sensory and motor block did not vary significantly in bupivacaine – clonidine and bupivacaine alone groups. Casati A¹³ evaluated the effects of clonidine 1 mcg / kg added to ropivacaine and concluded that the readiness required for surgery was 15 min (5-36 min) with ropivacaine group and 20 min (5 – 30 min) in clonidine- ropivacaine group. In study by Kellika P, a statistically significant earlier onset of sensory and motor block was observed when clonidine was added in a dose of 1.5 µg/kg but a combination of lignocaine-bupivacaine was used.¹⁸ The faster onset of action of lignocaine may be one factor responsible for this difference in onset time. Bernard and Macarie evaluated the effects of adding 30-300 µg clonidine to lignocaine for axillary brachial plexus block which hastened the onset of the block and improved the efficacy of surgical anesthesia.¹⁴ There are reported differences in the effects of administration of low-dose clonidine on time of onset and efficacy of nerve block, which may be explained by differences in the type of nerve block, exact mixture injected, and technique used to perform the block (single injection versus multiple injections). The fact that clonidine does not decrease the onset time seen in the

studies above and in our study suggests that clonidine does not have any beneficial effect regarding the time taken to establish the block,

In the present study the duration of sensory analgesia was 466 ± 75 (min) in control group whereas it was 876 ± 221 (min) in clonidine group. The duration of motor block in control group (bupivacaine) was 426 ± 72 (min) compared to 830 ± 214 (min) in clonidine group. The study showed a significant prolongation of sensory anesthesia with clonidine (7 hr) as adjunct to bupivacaine in dose of 2 mcg / kg as well as duration of motor blockade.

The results are consistent with the previous studies. Both Singelyn et al¹⁹ and El Saied et al²⁰ observed a 4hr prolongation of sensory analgesia with clonidine 1.5 mcg / kg (mepivacaine) and 150 mcg (ropivacaine) respectively. Casati A et al showed that 1 mcg/ kg body weight clonidine added to ropivacaine had sensory analgesia that lasted 15.2 hr compared to 13.8 hr in ropivacaine alone.¹³ He noted a 3 hr delay in the first analgesic request in the groups. Duma A et al observed a delay of 4 hr (mean) with clonidine for first analgesic request.¹⁷ He observed a maximum prolongation of sensory analgesia of upto 8 hrs (levo bupivacaine). Kelika P et al compared the peripheral nerve block enhancing properties of tramadol and two different doses of clonidine. The time for rescue analgesia was the longest (statistically significant) in patients who received 1.5 $\mu\text{g}/\text{kg}$ of clonidine.¹⁸ The increase was by an average of 3 h when compared with tramadol and 21 min when compared with 1 $\mu\text{g}/\text{kg}$ clonidine. This dose thus provided the maximum postoperative analgesia out of three doses. The present study showed a significant prolongation of sensory analgesia (7 hr). This shows that the dose of clonidine 2 mcg/kg is appropriate in its effects added to bupivacaine and has much additive effects on bupivacaine. Iohom et al also found that when clonidine added to mepivacaine for axillary brachial plexus block enhances both anesthesia and postoperative analgesia.²¹ Similarly Chakraborty et al used 30 μg of clonidine as an adjuvant to 0.5% bupivacaine for supraclavicular brachial plexus block and found prolonged postoperative analgesia.²²

The present study showed that the severity of pain at the requirement of analgesia was significantly lower ($p < 0.001$) in clonidine (2 mcg/kg) group compared with bupivacaine alone while Casati A et al observed the degree of pain measured at first analgesic request was similar in clonidine group (1 mcg/kg) added to ropivacaine and ropivacaine alone.¹³ Casati A et al used only 1 mcg/kg clonidine and have not found any beneficial effect on pain score while in the present study clonidine was used in dosage of 2 mcg/kg.

Sia S et al. administered clonidine as a sole analgesic in axillary block and found that it does not affect postoperative pain.²³ Butterworth JF studied that clonidine inhibit the action potential of A and C fibers in de-sheathed sciatic nerves.⁹ Clonidine exerts its local anesthetic-prolonging effect directly on the nerve fiber, as there is complex interaction between clonidine and axonal ion channels or receptors.²⁴ Peripheral antinociception induced by clonidine is due to alpha2-adrenoceptor-mediated local release of enkephalin-like substances.²⁵

Clonidine, an anti hypertensive agent has been found to cause hypotension when used as an adjunct in intrathecal route and sedation and dryness of mouth have also been noted.²⁶ Significant decrease in heart rate and blood pressure have been noted when used in epidural route. ²⁷Adnan T et al found that clonidine 150 mcg decreases heart rate, blood pressure and produce sedation apart from prolonging blockade when used as adjuvant for lidocaine in axillary block in chronic renal failure patients²⁸ while El Saied AH et al reported that same dose of clonidine when used as adjuvant for ropivacaine in axillary block prolongs blockade without significant changes in

onset of action, heart rate, blood pressure and sedation.²⁰ Bernard et al observed significant side effects with clonidine 300 mcg.⁹ The present study showed no incidences of hypotension, bradycardia, respiratory depression consistent with the study of El Saied AH et al. This may contribute to the fact that the dose used in the study was appropriate and clonidine does not produce any adverse effects when used in peripheral nerve blocks. However, Filos K S et al²⁶ and Motsch J et al²⁷ found hypotension, bradycardia possibly may be part of spinal anesthesia.

Mild sedation was observed in 5 patients out of 30 patients who received clonidine. There was no incidence of any respiratory depression and the patients were easily arousable on command. So this minor degree of sedation need not be considered as a major side effect. These findings are consistent with other studies by Kelika P et al.¹⁸ Hrishi et al also found that Intraoperative sedation scores were higher in the clonidine group when compared with the control group but were not statistically significant.²⁹

CONCLUSION

Clonidine at the dose of 2 mcg / kg body weight added to 0.5% bupivacaine in supraclavicular brachial plexus block in upper limb surgeries is highly effective in prolongation of sensory analgesia and provides a better post operative period for the patient free of pain without any potential side effects.

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