Original Article

Clonidine as an adjuvant to bupivacaine in infraclavicular brachial plexus block for prolongation of post-operative analgesia

K Sri Hyndavi[1*], Divakar Patil[2], Abhijit Mohite[3], Rajesh Navale[4], Jyotsna Paranjpe[5]

[1,3]PG Student, [2,5]Professor, [4]Sr. Resident, Department of Anaesthesiology, BVDU Medical College and Hospital, Sangli, Maharashtra, INDIA.
Email: ksrihyndavi@yahoo.com

Abstract

Background: Brachial plexus block is the ideal anaesthetic technique for upper limb surgeries. Several clinical studies have shown that Clonidine when used as an adjuvant to bupivacaine prolongs sensory and motor blockade. **Aims and Objectives:** To evaluate the effect of this combination of drugs with respect to the onset, duration of sensory and motor blockade and duration of analgesia in Infra-clavicular brachial plexus block for elective upper limb orthopedic surgeries. **Material and Methods:** In this prospective, randomized double-blind placebo controlled study, 40 patients of American Society of Anaesthesiologists Grade I or II undergoing elective upper limb orthopedic procedures through Infra-clavicular approach for brachial plexus block were randomly divided into two groups. **Group C** received 30ml of 0.375% Bupivacaine and 0.4ml normal saline (n=20) **Group S** received 30ml of 0.375% Bupivacaine and (60µg) clonidine (n=20). Both the groups were compared for onset and duration of sensory and motor block, postoperative analgesia, level of sedation, side-effects and complications. **Results:** Analgesia duration was 753.2±109.6 min (mean ± standard deviation) in group S (clonidine) compared to 210.2±32.min in group C (control). Onset time was shorter while duration of sensory and motor blockade were longer in group S(clonidine) than group C(control) and the difference was statistically significant. No clinical significance was observed in hemodynamics. Ramsay Sedation Score (RSS) was higher in the group S(clonidine) group. **Conclusion:** Addition of small dose of clonidine (60µg) to bupivacaine shortens the onset time and prolongs the duration of sensory and motor blockade and duration of post operative analgesia significantly without any major side effects other than sedation which is beneficial in clinical practice.

Keywords: Clonidine, Bupivacaine, Infraclavicular brachial plexus block, Duration of analgesia, Randomized controlled trial, Ramsay sedation score.

[*]**Address for Correspondence:**
Dr. K. Sri Hyndavi, PG Student, Department of Anaesthesiology, BVDU Medical College and Hospital, Sangli,-416414, Maharashtra, INDIA.
Email: ksrihyndavi@yahoo.com
Received Date: 16/12/2015 Revised Date: 20/01/2016 Accepted Date: 12/02/2016

Access this article online	
Quick Response Code:	Website: www.statperson.com
	DOI: 18 March 2016

INTRODUCTION

Peripheral nerve blocks have assumed a prominent role in modern anesthesia practice as they provide ideal operative conditions without any sedation or systemic hemodynamic effects.[1] Brachial plexus block (BPB) is a commonly used regional anesthetic technique for surgeries involving upper limb, especially orthopedic procedures. The infraclavicular BPB with coracoid approach has gained popularity because of its consistent bony landmarks, less chances of vascular puncture, pneumothorax and adequate neural blockade.[2] Success rate of the block can be further enhanced by using electric nerve stimulator to identify the nerves and depositing the drug perineurally.[3] Many adjuvants like adrenaline, dextran 10%, potassium chloride, clonidine, dexmeditomidine, dexamethasone, neostigmine and opioids,[4-12] has been added to local anesthetics to improve onset and duration of block, to decrease postoperative analgesic requirement and to reduce systemic effects in brachial plexus blockade. Clonidine, a selective α_2 adrenergic agonist inhibits nocioceptive impulses by activating postjunctional α_2 adrenoreceptors both at

How to site this article: K Sri Hyndavi, Divakar Patil, Abhijit Mohite, Rajesh Navale, Jyotsna Paranjpe. Clonidine as an adjuvant to bupivacaine in infraclavicular brachial plexus block for prolongation of post-operative analgesia. *International Journal of Recent Trends in Science and Technology*. March 2016; 18(2): 368-372. http://www.statperson.com (accessed 20 March 2016).

peripheral and spinal nerve endings. It is, however, not free of adverse effects, the most commonly observed being dry mouth, sedation, hypotension, and bradycardia.[13,14] Sedative properties of clonidine are attributable to its lipophilic nature resulting in systemic absorption when administered perineurally.[13] The present study was designed to evaluate the effect of adding 60µg clonidine to bupivacaine with regards to onset and duration of sensory and motor blockade, hemodynamic variables, postoperative analgesia, and adverse effects.

MATERIAL AND METHODS

The study protocol of this prospective, randomized, double-blinded, placebo-controlled trial was approved by the Hospital Ethics Committee. All participants gave written informed consent. Forty patients, ASA physical status I–II in the age group of 18-65 of either sex scheduled for elective upper limb surgery were randomly allocated into two groups each of 20 by chit in box method:

Group C: (control) received 30ml of 0.375% Bupivacaine and 0.4ml normal saline (n=20)

Group S: (study) received 30ml of 0.375% Bupivacaine and (60µg) clonidine (n=20)

Patients who had local pathology at the site of injection or disability, history of convulsion, allergy to the study drugs used, bleeding disorders, uncooperative and with significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal or hepatic diseases, pregnant or lactating women, morbid obesity and patients receiving chronic analgesic therapy and those with inadequate block and contraindications to regional anesthesia were excluded from the study. A detailed preanesthetic check-up of the patients was carried out a day before surgery. General physical examination and systemic examination was done. Routine investigations were reviewed. Premedication was given with tabl*et al*prazolam 0.25 mg orally at 22:00 h on the night before surgery and at 06:00 h on the morning of the surgery. No additional sedative medication was administered in the first 60 min after injection of the study dose. The interpretation of the visual analogue scale (VAS) was explained to the patients to determine the level of analgesia in the intra and postoperative period. This was carried out with a 10 cm line. The 1st end marked "0" means "no pain" and end marked "10" means "severe pain." On the day of surgery, patients were shifted to operation theatre and fasting status, consent and PAC were checked and intravenous (i/v) access was gained with 18‑gauge canula. Patients were preloaded with 10 ml/kg body weight of Ringer lactate solution over 15–20 min. Multipara monitor was attached to the patients to record base line respiratory rate, pulse rate, noninvasive systolic and diastolic blood pressure, SpO2 and electrocardiogram (ECG). Patients were made to lie in the supine position with the head facing away from the side to be blocked. Brachial plexus block was administered to all the patients by infraclavicular approach with the help of a nerve stimulator. The coracoids process was located and the needle entry point, 2 cm medial and 2 cm caudal to the most prominent part of the coracoids process was marked. After appropriate skin preparation, local anesthetic (lignocaine 2%) was infiltrated at the needle insertion site. A 22‑gauge, 50 mm insulated short bevelled needle was introduced vertically at the specified land mark, with nerve stimulator set at a current of 1mA and frequency of 2Hz. As the nerve was approached movement of the wrist or fingers were elicited and then the current was gradually reduced to 0.4 mA. When hand twitches were elicited at a current of 0.4 mA, it was taken as the end point, and the study drug was given in 5 ml incremental doses after aspiration before each dose to avoid intravascular injection. Patients in group S received 30 ml of 0.375% Bupivacaine plus 0.4 ml (60 µg) clonidine and patients in group C received 30 ml of 0.375% bupivacaine plus 0.4 ml normal saline. The study drugs were prepared by a separate anesthesiologist in an identical syringes, and the volume of the drug was also kept constant to avoid bias. Anesthesiologist performing the block was unaware of the drug used. Same anesthesiologist also monitored all the variables throughout the study. Oxygen was routinely administered via oxygen mask at 4 L/min after performing the block. Patients were monitored for block characteristics, hemodynamic parameters and side‑effects and complications. All durations were calculated considering the time of administering the block as time 0. Block was considered successful when at least 2 out of 4 nerve territories (ulnar, radial, median, musculocutaneous) were blocked effectively for both sensory and motor. The onset of sensory block was evaluated by 3 point sensory score by pin prick method. 0 – normal sensation, 1 – analgesia (loss of pin prick sensation), 2 – anesthesia (loss of touch) Assessment of motor blockade was done using 3 point modified Bromage score[15] 0 - motor function with full extension and flexion of elbow, wrist, and fingers,[1] − decreased motor strength, with ability to move only fingers, 2 − complete motor block with inability to move elbow, wrist, and fingers. Both intraoperative and postoperative sedation was rated by using the Ramsay sedation score, 1) Anxious or restless or both, 2) Cooperative, oriented and tranquil, 3) Responds to commands, 4) Brisk response to stimulus, 5 – sluggish response to stimulus, 6 – no response to stimulus. Both sensory and motor blocks were assessed every 3 min till their onset and at 15, 30, 45, 60, 120min

and hourly (even after surgery) until they had resolved. Hemodynamic parameters were also recorded at the above said time. Postoperative pain was assessed using the visual analog scale (VAS) (0 – no pain to 10 − worst pain)[16] every hour till the block lasted. The end-point of the study was time from performance of the block to the onset of pain as determined by VAS score of 4 or more. Rescue analgesia was provided with tramadol 2 mg/kg intravenous (IV). Patients were observed for any discomfort, nausea, vomiting, shivering, bradycardia, pain and any other side-effects. Any need for additional medication was noted. Blood loss during surgery was replaced with blood if it was more than the maximum allowable blood
loss.

RESULTS

Results were expressed as mean± SD (SEM). Demographic and hemodynamic data were compiled and subjected to statistical analysis using Statistical Packaging for Social Sciences (SPSS), version 15. In the present study, both groups were comparable with respect to the demographic profile ($P > 0.05$) as shown in Table 1.

Table 1:

	GROUP S (n=20) X ± SD	GROUP C (n=20) X ± SD	p value
Age (years)	30.4 ± 9.9	30.8 ± 10.7	> 0.05
Height (cm)	167.8 ± 9.2	168.5 ± 10.0	> 0.05
Weight (kg)	59.3 ± 6.8	61.3 ± 7.4	> 0.05
Gender (M/F)	12 / 8	11 / 9	> 0.05

P value < 0.05 is considered statistically significant

Table 2: Characteristics of sensory and motor block in both the groups

Time (min)	GROUP S (n=20) X ± SD	GROUP C (n=20) X ± SD	t - value	p - value
Onset time sensory block (osb)	14.7 ± 1.6	21.3 ± 2.7	9.4046	< 0.0001
Onset time motor block (omb)	17.4 ± 1.5	24.6 ± 3.0	9.6000	< 0.0001
Duration time sensory block (dsb)	690 ± 91.7	229 ± 49.5	19.7842	< 0.0001
Duration time motor block (dmb)	598.0 ± 103.2	202.3 ± 30.6	16.4400	< 0.0001
Duration of analgesia (doa)	753.2 ± 109.6	232.7 ± 57.4	18.8145	< 0.0001

Comparison of different variables

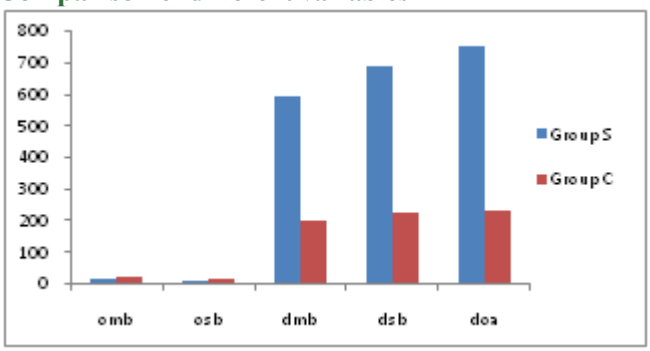

Figure 1: Time (min) Changes in Heart Rate

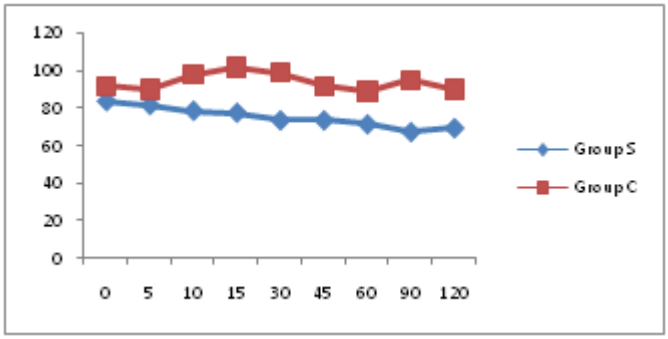

Figure 2: Bpm Changes in SBP and DBP

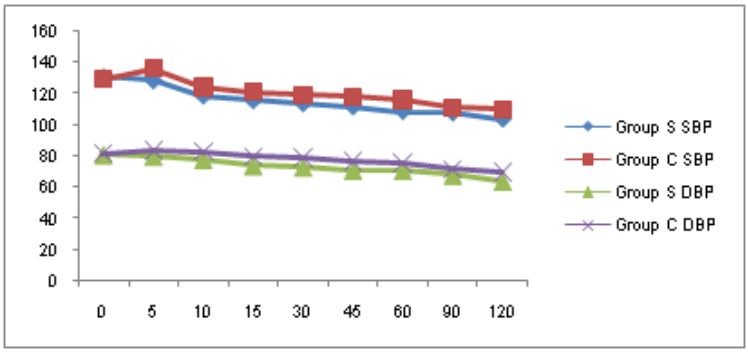

Figure 3: BP (mm of Hg)

DISCUSSION

Infraclavicular BPB offers certain advantages over supraclavicular and interscalene approaches as the complications like pneumothorax and vascular puncture are less, and the block is more consistent.[17] The coracoids approach for infraclavicular block is still better, as the coracoid process is easy to identify, and no limb movement is required.[18] Clonidine and local anaesthetic agents have a synergistic action. Clonidine enhances both sensory and motor blockade of neuraxial and peripheral nerves after injection of local anaesthetic solution. In the present study, brachial plexus blockade was achieved by infraclavicular approach and satisfactory surgical anesthesia was attained in all the cases for various types

of upper limb surgeries. Clonidine, when added to bupivacaine, was found to be superior to bupivacaine alone. Various studies were done where clonidine was used as an adjuvant to bupivacaine and block characteristics were compared with plain bupivacaine and it was found that addition of clonidine leads to faster onset and prolonged duration of sensory and motor block with improved analgesia.[26-29] Both Bernard and Macaire[23] and Iohom *et al*.,[25] have reported a faster onset of sensorimotor block with the use of clonidine as an adjuvant to LA than plain LA. We also found an enhancement of perioperative analgesia and prolongation of recovery of sensation in the clonidine group, well beyond the pharmacological effect of either clonidine or bupivacaine. Direct modulation of the activity of sensory nerve fibres could conceivably explain the difference between the two groups in our study. Alternatively, this could have been a result of an overall better quality of anaesthesia at all times of surgery. Regardless of the mechanism, clonidine was found to have a valuable advantage in the field of peripheral nerve blocks when added to bupivacaine. Most of the studies conducted using clonidine in regional anaesthesia did not report any adverse effects.[23] Ghoshmaulik *et al*.,[30] concluded that 150 µg clonidine used as an adjuvant to 30 ml of 0.5% bupivacaine resulted in prolongation of sensory block (625 ± 35 min), motor block (690 ± 38 min) and duration of analgesia (930 ± 45 min) without any significant hemodynamic variability. However, studies by Buttner *et al*. and Bernard *et al.* reported the incidence of hypotension and bradycardia with the use of clonidine.[24,25] In our study, no side-effects were observed in both the clonidine and the control group throughout the study period.

CONCLUSION

To summarize, our study suggests that clonidine 60µg in 30 ml of 0.375% bupivacaine significantly enhances the quality of infraclavicular brachial plexus block in upper limb surgeries by a faster onset and prolonged duration of sensory and motor block, enhancing post-operative analgesia. These benefits are not associated with any hemodynamic changes or other adverse effects. In conclusion, clonidine added to bupivacaine is an attractive option for improving the quality and duration of infraclavicular brachial plexus block in upper limb surgeries.

REFERENCES

1. Khanduri KC. Regional anaesthetic techniques for orthopaedic surgeries. Med J Armed Forces India 2008; 64:109.
2. Wilson JL, Brown DL, Wong GY, Ehman RL, Cahill DR. Infraclavicular brachial plexus block: Parasagittal anatomy important to the coracoid technique. Anesth Analg 1998; 87:870‑3.
3. Eeckelaert JP, Filliers E, Alleman JJ, Hanegreefs G. Supraclavicular brachial plexus block with the aid of a nerve stimulator. Acta Anaesthesiol Belg 1984; 35:5‑17.
4. Murphy DB, McCartney CJ, Chan VW. Novel analgesic adjuncts for brachial plexus block: A systematic review. Anesth Analg 2000; 90:1122-8.
5. Gormley WP, Hill DA, Murray JM, Fee JP. The effect of alkalinisation of lignocaine on axillary brachial plexus anaesthesia. Anaesthesia 1996; 51:185-8.
6. Bazin JE, Massoni C, Bruelle P, Fenies V, Groslier D, Schoeffl er P. The addition of opioids to local anaesthetics in brachial plexus block: The comparative effects of morphine, buprenorphine and sufentanil. Anaesthesia 1997; 52:858-62.
7. Bone HG, Van Aken H, Booke M, Bürkle H. Enhancement of axillary brachial plexus block anesthesia by coadministration of neostigmine. Reg Anesth Pain Med 1999; 24:405-10.
8. Kapral S, Gollmann G, Waltl B, Likar R, Sladen RN, Weinstabl C, et al. Tramadol added to mepivacaine prolongs the duration of an axillary brachial plexus blockade. Anesth Analg 1999; 88:853-6.
9. Karakaya D, Büyükgöz F, Baris S, Güldogus F, Tür A. Addition of fentanyl to bupivacaine prolongs anesthesia and analgesia in axillary brachial plexus block. Reg Anesth Pain Med 2001; 26:434-8.
10. Keeler JF, Simpson KH, Ellis FR, Kay SP. Effect of addition of hyaluronidase to bupivacaine during axillary brachial plexus block. Br J Anaesth 1992; 68:68-71.
11. Khosa DS, Thind SS, Gupta HK, Jain S. Effect of adding potassium chloride to lignocaine and bupivacaine solution on the onset time and duration of brachial plexus block. Indian J Anaesth 1990; 38:119-22.
12. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. Anesth Analg 2006; 102:263-7.
13. McCartney CJ, Duggan E, Apatu E. Should we add clonidine to local anesthetic for peripheral nerve blockade? A qualitative systematic review of the literature. Reg Anesth Pain Med 2007; 32:330‑8.
14. Culebras X, Van Gessel E, Hoffmeyer P, Gamulin Z. Clonidine combined with a long acting local anesthetic does not prolong postoperative analgesia after brachial plexus block but does induce hemodynamic changes. Anesth Analg 2001; 92:199‑204.
15. Gaumann D, Forster A, Griessen M, Habre W, Poinsot O, Della Santa D. Comparison between clonidine and epinephrine admixture to lidocaine in brachial plexus block. Anesth Analg 1992; 75:69‑74.
16. Singelyn FJ, Gouverneur JM, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg 1996; 83:1046‑50.
17. Raj PP, Montgomery SJ, Nettles D, Jenkins MT. Infraclavicular brachial plexus block – a new approach. Anesth Analg 1973; 52:897‑904.
18. Trehan V, Srivastava U, Kumar A, Saxena S, Singh CS, Darolia A. Comparison of two approaches of infraclavicular brachial plexus block for orthopaedic

surgery below mid‐humerus. Indian J Anaesth 2010; 54:210‐4.
19. El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boulis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth 2009; 103:268-74.
20. Bhatnagar S, Mishra S, Madhurima S, Gurjar M, Mondal AS. Clonidine as an analgesic adjuvant to continuous paravertebral bupivacaine for post-thoracotomy pain. Anaesth Intensive Care 2006; 34:586-91.
21. Gabriel JS, Gordin V. Alpha 2 agonists in regional anesthesia and analgesia. Curr Opin Anaesthesiol 2001; 14:751-3.
22. Singelyn FJ, Dangoisse M, Bartholomee S, Gouverneur JM. Adding clonidine to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Reg Anesth 1992; 17:148-50.
23. Bernard JM, Macaire P. Dose-range effects of clonidine added to lidocaine for brachialplexus block. Anesthesiology 1997; 87:277-84.
24. Buttner J, Ott B, Klose R. The effect of adding clonidine to mepivacaine. Axillary brachial plexus blockade. Anaesthesist 1992; 41:548-54.
25. Iohom G, Machmachi A, Diarra DP, Khatouf M, Boileau S, Dap F, et al. The effects of clonidine added to mepivacaine for paronychia surgery under axillary brachial plexus block. Anesth Analg 2005; 100:1179‐83.
26. Chakraborty S, Chakrabarti J, Mandal MC, Hazra A, Das S. Effect of clonidine as adjuvant in bupivacaine‐induced supraclavicular brachial plexus block: A randomized controlled trial. Indian J Pharmacol 2010; 42:74‐7.
27. Singh S, Aggarwal A. A randomized controlled double‐blinded prospective study of the efficacy of clonidine added to bupivacaine as compared with bupivacaine alone used in supraclavicular brachial plexus block for upper limb surgeries. Indian J Anaesth 2010; 54:552‐7.
28. Paliwal B, Karnawat R. Comparative study of effects of buprenorhpine or clonidine as adjuvants to local anesthetics (bupivacaine 0.25%) for supraclavicular brachial plexus block. IOSR J Dent Med Sci 2013; 4:30‐8.
29. Kulkarni A, Tarkase AS, Chaudhari SA. Effects of addition of clonidine to bupivacaine in brachial plexus block. Pravara Med Rev 2012; 4:15‐9.
30. Ghoshmaulik S, Bisui B, Saha D, Swaika S, Ghosh AK. Clonidine as an adjuvant in axillary brachial plexus block for below elbow orthopaedic surgeries: A comparison between local and systemic administration. Anesth Essays Res 2012; 6:184-8.

Source of Support: None Declared
Conflict of Interest: None Declared