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Clonidine as an Adjuvant in Axillary Brachial Plexus Block for Below Elbow Orthopedic Surgeries: A Comparison Between Local and Systemic Administration

Dr.Parul N. Panchotiya	Associate professor of anesthesia department, V.S. General hospital,Ahmedabad.
Dr.Hardik Bansikumar Modi	3 rd year resident of anesthesia, V.S. General hospital,Ahmedabad.
Dr.Subhashchandra shyobaksharam Gora	2 nd year resident of anesthesia, V.S. General hospital,Ahmedabad.
Dr. Kuntal Revabhai Patel	2 nd year resident of anesthesia, V.S. General hospital,Ahmedabad.

ABSTRACT

Background: Axillary brachial plexus block for below elbow orthopedic surgery provides a safe and low-cost technique with the advantage of prolonged postoperative analgesia. Clonidine, with selective partial agonist activity on adrenergic receptors, has significantly demonstrated its role in this regard as an adjuvant to local anesthetics.The current study compares the locally administered clonidine with systemically administered control group in terms of onset and duration of sensory block, motor block, and analgesia; hemodynamic variability; sedation; and other side effect profile.

Materials and Methods: Seventy patients (ASA I or II) scheduled for below elbow orthopedic surgeries were randomly allocated in equal numbers to receive either 30 ml of 0.5% plain bupivacaine with 150 g (1 ml) of inj. clonidine locally in the axillary sheath and 1 ml of normal saline (NS) subcutaneously (Group L) or 30 ml of 0.5% plain bupivacaine with 1 ml of NS locally and 150 g (1 ml) of inj. clonidine subcutaneously (Group S). Standard monitoring of vital parameters was done. Duration of sensory and motor block, analgesia, hemodynamic changes, and any adverse effects were observed and recorded for different duration up to 24 h.

Results: Duration of sensory block (625 ± 35 min), motor block (690 ± 38 min), and analgesia (930 ± 45 min) was significantly longer in Group L than in Group S [sensory block (480 ± 30 min), motor block (535 ± 25 min), and analgesia (720 ± 30 min)] ($P < 0.05$). Significant alteration of heart rate, systolic blood pressure and diastolic blood pressure, and mean arterial pressure in Group S was observed compared to Group L ($P < 0.05$). Side effects like nausea and vomiting were comparable,but highly significant sedation score ($\chi^2 = 47.75$ and 49.51 at 120 and 240 min, respectively;$P < 0.01$) was observed between the two groups.

Conclusion:Compared to systemic administration,local clonidine as an adjuvant in axillary block resulted in significant prolongation of duration of sensory and motor blockade, and analgesia without any hemodynamic alteration, probably by locally mediated mechanism of action.

KEYWORDS Adjuvant, axillary block, clonidine, local, systemic

INTRODUCTION

Axillary brachial plexus block for below elbow orthopedic surgeries provides a safe and low-cost technique with the advantage of prolonged postoperative analgesia.[1] Various adjuvants to local anesthetics like epinephrine, opioids, neostigmine, tramadol, and recently clonidine have been studied for their efficacy in lengthening the pain-free period.[2] Clonidine, an imidazoline with selective partial agonist activity on α_2 adrenergic receptors, has significantly demonstrated its role in this regard.[3] This effect could be mediated through direct inhibition of C-fiber and Aβ fiber action potential, with little effect on Aβ fibers as reflected by the lack of motor or sensory block to light touch when used as a sole analgesic agent.[1,4,5] Although systemic administration of clonidine is associated with potentiation of spinal anesthesia in the postoperative period,[6] it is associated with significant hemodynamic alterations like bradycardia and hypotension as well as central nervous system (CNS) effects like sedation.[3]

Most of the studies conducted till date has established the role of clonidine as an adjuvant to local anesthetics when administered at the site of peripheral nerve blocks. Adequate comparison with systemically administered clonidine is necessary to substantiate its role as a locally administrable adjuvant in peripheral nerve blocks.[2] The current study was planned with the aim of comparing locally administered clonidine with systemic control group in terms of the following:

I. Onset and duration of sensory and motor block
II. Duration of analgesia
III. Hemodynamic variability
IV. Sedation and other side effect profile

MATERIALS AND METHODS

After obtaining clearance from the Institutional Ethics Committee and written informed consent from the participants, 70 ASA I or II patients aged between 20 and 60 years of either sex, scheduled to undergo elective below elbow orthopedic surgeries in Burdwan Medical College and Hospital, were selected and randomly allocated into two equal groups, namely, group (Gr) S (n = 35) and Gr L (n = 35), by computerized randomization. Exclusion criteria included h/o hypertension and ischemic heart disease (IHD), peripheral neuropathy, pulmonary, hepatic, and renal diseases, h/o hypersensitivity to local anesthetics, those receiving anticoagulants, psychotropic medicines, or adrenergic agonists, as well as

pregnant and lactating woman, and patients having substance abuse. Gr L received 30 ml of 0.5% plain bupivacaine with 150 mg (1 ml) of inj. clonidine locally in the axillary sheath and 1 ml of normal saline (NS) subcutaneously. Gr S received 30 ml of 0.5% plain bupivacaine with 1 ml of NS locally while 150 mg (1 ml) of inj. clonidine was administered subcutaneously. Rescue analgesic was standardized as 50 mg inj. diclofenac to be given when demanded. The drugs were prepared by an anesthesiologist not included in the study and the observations were made by another person unaware of the type of drug received by an individual patient.

All patients received 5 mg of tab. diazepam on the night before operation and no other premedication subsequently. After establishing intravenous access on arrival in the operating room, they were administered the axillary brachial plexus block by the same anesthesiologist using a standard block technique for perivascular approach. At the same time of block administration, the patients received subcutaneous injection of 1 ml containing either the study drug or NS as per the protocol. Monitoring with Kopran® multipara monitor, starting from before administration of the block till 120 min after completion of the block, was done for heart rate (HR), oxygen saturation (SPO), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP), and the recordings were taken at 0, 5, 10, 30, 60, and 120 min.

Patients were assessed for onset of sensory and motor block every 5 min for 40 min. Sensory block of ulnar, median, and radial nerves was determined by pinprick along the distribution of each nerve and compared to the same stimulation on contralateral arm. Using a scale of 0 (complete sensory blockade) to 100 (no sensory blockade), patients were requested to quantify the degree of sensory block. Sensory block onset was defined as 30 or less in the said scale and the time was recorded for each nerve to eliminate the error of differential blockade.[7] Motor block was assessed by thumb abduction (radial), thumb adduction (ulnar), and thumb opposition (median), using a modified Bromage Scale[1] (3 = extension of elbow against gravity, 2 = flexion of wrist against gravity, 1 = finger movement, 0 = no movement). Motor block onset was defined as reduction of muscle power to 3 or less and the time from block administration was recorded. Duration of sensory block was determined till the complete recovery of sensation, while that of motor block was determined till the recovery of full muscle power. Analgesia was assessed using a 3-point scale for pain using pinprick with 23-G needle (2 = sharp pain, 1 = blunt pain, 0 = no pain).[1] Duration of analgesia was determined till the patient's demand for rescue analgesic. The duration of blockade and that of analgesia were recorded at 120, 180, 240, 360, and 480 min from block administration. Any significant intraoperative hypotension or bradycardia (>20% change), as well as nausea, vomiting, and other side effects were also noted. Sedation was assessed at 120, 240, and 360 min using a 4-point scale (1 = awake, 2 = drowsy but responsive to command, 3 = very drowsy but responsive to pain, 4 = unresponsive).[1] At the end of operation, the patients were requested to note the time of full recovery of sensation and muscle power and the nursing staff was requested to note the time of rescue analgesic, which was subsequently verified by the observer.

Sample size was determined from previous studies.[1,7,8] Assuming 20% increase in the duration of blockade and analgesia as clinically significant with a power of 80, the sample size at 10% level of significance was 64. In this study, 70 patients (n = 35 in each group) were selected. Results are expressed as Mean ± SEM/SD. Patient characteristics and times were analyzed for normality and two groups were compared using unpaired t-tests.

Nonparametric data were analyzed using Chi-square test (χ^2). A P value <0.05 was considered statistically significant.

RESULTS

Of the 70 patients selected, failure of block was observed in 5 patients (2 in Gr L and 3 in Gr S); hence, the results were compared in 65 patients. Both the groups were comparable in demographic profile and duration of surgery [Table 1]. The onset of sensory and motor block between the two groups yielded no significant difference. Significant prolongation of duration of sensory block in Gr L (625 ± 35 min) was observed compared to Gr S (480 ± 30 min) (P < 0.05). Similar prolongation of motor block was observed (690 ± 38 min in Gr L vs. 535 ± 25 min in Gr S; P < 0.05). Analgesia duration in Gr L (930 ± 45 min) was significantly prolonged than that in Gr S (720 ± 30 min) (P < 0.05). Analgesia score at 240 min was significantly lower in Gr L (P < 0.05), but this difference became highly significant (P < 0.01) at 360 and 480 min, thus emphasizing the prolonged postoperative analgesia in local clonidine group [Table 2]. Among the hemodynamic parameters, significant differences in HR, SBP, DBP, and MAP were observed in Gr S compared to Gr L, mostly after 30 min of administration of the drug [Table 3]. These changes persisted even at 120 min. The sedation scores at 120 and 240 min were significantly higher in Gr S than in Gr L (P < 0.01) [Table 4]. However, they were comparable at 360 min. Both the groups were comparable in their side effect profile.

DISCUSSION

Systematic review of various adjuvant in axillary brachial plexus block suggests that compared to others, clonidine appears to have greater analgesic benefit with minimal adverse effects. However, studies comparing clonidine as an adjuvant to local anesthetic with a systemic control group are lacking.[2] This study fairly meets the above requirement. An arbitrary dose of 150 mg of clonidine[9,10] to 30 ml of 0.5% plain bupivacaine resulted in significant prolongation of sensory block (625 ± 35 min), motor block (690 ± 38 min), and duration of analgesia (930 ± 45 min), without any significant hemodynamic variability in the locally administered group [Figures 1-3]. On the other hand, the systemic control group showed significant alterations in hemodynamic parameters without any prolongation of anesthesia and analgesia compared to bupivacaine alone group in other studies.[8]

Studies emphasizing clonidine as an adjuvant for prolongation of spinal anesthesia and peripheral nerve blocks are well established.[1,11,12] Again, oral clonidine also Nonparametric data were analyzed using Chi-square test (c^2). A P value <0.05 was considered statistically significant.

Table 1: Demographic data and duration of surgery Parameter

Parameter	Gr S	Gr L
Sex (F/M)	12/20	14/19
Age (years)*	40±11	42±10
Body weight (kg)*	56±12	58±10
Duration of surgery* (min)	89.5±10.5	95.8±12.3
*Values are Mean±SD, P>0.05		

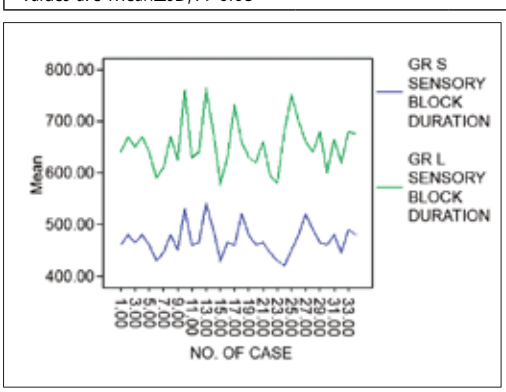

Figure 1: Duration of sensory block

Table 2: Comparison of anesthesia and analgesia parameters

Parameter	Onset of sensory block			Onset of motor block analgesia	Duration of sensory block	Duration of motor block	Duration of analgesia	Analgesia score		
	Ulnar	Median	Radial					240 min	360 min	480 min
Gr S	17±1.3	18.5±1.5	20±1.8	28±2.5	480±30	535±25	720±30	0-26, 1-6	0-4, 1-28	1-9, 2-
23 Gr L		19.5±1.5	21.5±1.9	24.9±1.7	26±1.7	625±35*		690±38*	930±45*	0-32, 1-
1	0-291-4			1-28, 2-5						
P value	>0.05	>0.05	>0.05	>0.05	<0.05	<0.05	<0.05	χ^2-5.10* <0.05	χ^2-46.28** <0.01	χ^2-26.51** <0.01

*Significant; **highly significant Parametric values are Mean±SEM. Nonparametric data from Chi-square test (χ^2)

Table 3: Hemodynamic variability between two groups

Time (min)	Heart rate		Systolic blood pressure		Diastolic blood pressure		Mean arterial pressure	
	Gr S	Gr L	Gr S	Gr L	Gr S	Gr L	Gr S	Gr L
0	83±1.34	82.8±1.32	126±1.61	124±1.7	78.7±1.04	77.5±1.1	96.95±1.21	93±1.2
5	80.5±1.27	82.6±1.34	124.2±1.57	120±1.1	77.8±1.37	75.9±1.14	94.3±1.42	90.8±1.36
10	74.3±1.31	78.4±1.31	117.9±1.13	121.76±1.15	75±1.1	73.76±1.24	89±1.16	89.76±1.28
30	65.6±1.33*	75.2±1.29	97±1.1*	114±1.24	62.4±1.18*	72.2±1.1	57±1.36*	86.1±1.34
60	64.6±1.35*	75.8±1.33	97.3±1.24*	112.64±1.22	62.4±1.21*	74.6±1.26	63.2±1.18*	87.28±1.18
120	65.8±1.29*	78.6±1.32	105±1.6*	124.32±1.6	64.4±1.32*	76.8±1.16	64.6±1.22*	92.44±1.44
Significance	*P<0.05		*P<0.05		*P<0.05		*P<0.05	

Values are Mean±SEM; *Significant

Table 4: Comparison of sedation scores in the postoperative period

Time (min)	Gr S	Gr L	χ^2 test	*P* value	Significance
120	1-1, 2-9, 3-24	1-29, 2-3, 3-2	47.75	*P*<0.01	Highly significant
240	1-2, 2-21, 3-11	1-31, 2-2, 3-1	49.51	*P*<0.01	Highly significant
360	1-26, 2-3, 3-5	1-31, 2-2, 3-1	3.31	*P*>0.05	Insignificant

Values from nonparametric test (Chi-square test)

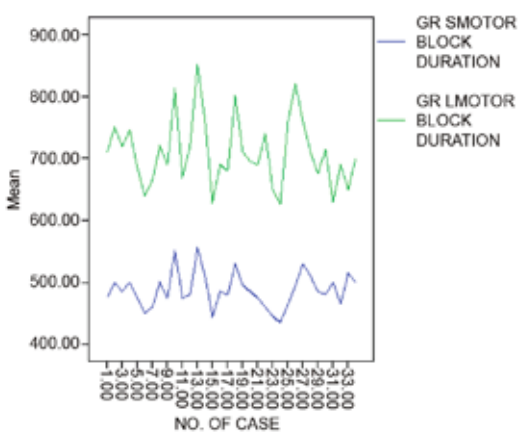

Figure 2:Duration of motor block

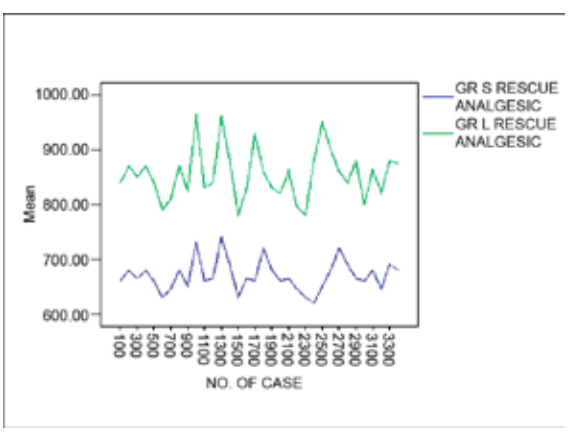

Figure 3:Duration of analgesia

prolongs the spinal block.[13,14] So, the question regarding the exact mechanism of action of clonidine for such analgesic action remains unanswered. High lipid solubility, quick crossing of blood brain barrier, and selective a2 receptor agonism at both spinal and supraspinal levels within the CNS producing the analgesic effect may be a possible explanation for the systemically administered group.[15,16] Comparable analgesia between systemic and local administration of clonidine as the sole analgesic in interscalene brachial plexus block suggests direct peripheral action of clonidine.[5] The enhancing effect of low-dose clonidine on lidocaine-induced inhibition of action potential of C-fibers and A fibers[4,17] together with synergistic mechanism of action with local anesthetics[1] may be the possible explanation to the direct peripheral action.

Addition of clonidine both locally and subcutaneously to mepivacaine plus epinephrine, when compared to mepivacaine-plus epinephrine alone demonstrated significant prolongation of duration of analgesia and anesthesia in the local group compared to the other two groups.[9] The current study results highly corroborate these findings.

The current study findings of significant alterations in HR, SBP,

DBP, and MAP, together with significant sedation in the systemic group outweigh the analgesic benefit of systemic administration of clonidine. The primary sympatholytic effect due to reduced peripheral norepinephrine release through stimulation of prejunctional inhibitory a2 receptors is responsible for the hemodynamic alteration like hypotension. Whereas bradycardia is an idiosyncratic reaction and sedation is the dose-dependent adverse effect of systemic clonidine administration. [18]

CONCLUSION

Clonidine, in a dose of 150 mg added locally to bupivacaine for axillary brachial plexus block, is an appropriate adjuvant for clinical practice although the exact mechanism of such an action is still speculative. This study also establishes the fact that compared to systemic administration; locally administered clonidine has definite advantage of prolongation of sensory and motor block as well as the duration of postoperative analgesia without significant hemodynamic instability and other systemic side effects like sedation.

REFERENCES

1. El Saied AH, Steyn MP, Ansermino JM. Clonidine prolongs the effect of ropivacaine for axillary brachial plexus blockade. Can J Anaesth 2000;47:962-7. | 2. Murphy DB,McCartney CJ,Chan VW Novel analgesic adjuncts for brachial plexus block: A systematic review.Anesth Analg 2000;90:1122-8. | 3. Maze M,Tranquilli W. Alpha 2 adrenoceptor agonists: Defining the role inclinical anesthesia.Anesthesiology 1991;74:581-605. | 4. Gaumann DM, Brunet PC, Jirounek P. Clonidine enhances the effect of lidocaine on C fiber action potential.Anesth Analg 1992;74:719-25. | 5. Iskandar H,Benard A,Ruel-Raymond J,Cochard G,Manaud B.The analgesic effect of interscalene block using clonidine as an analgesic for shoulder arthroscopy.Anesth Analg 2003;96:260-2. | 6. Liu S, Chui AA, Neal JM, Carpenter RL, Bainton BG, Gerancher JC. Oral clonidine prolongs lidocaine spinal anesthesia in human volunteers. Anesthesiology 1995;82:1353-9. | 7. Duma A, Urbanek B, Sitzwohl C, Kreiger A, Zimpfer M, Kapral S. As an adjuvant to local anaesthetic axillary brachial plexus block:A randomized, controlled study. Br J Anaesth 2005;94:112-16. | 8. Erlacher W, Schuschnig C, Koinig H, Marhofer P, Melischek M, Mayer N, et al.Clonidine as adjuvant for mepivacaine,ropivacaine and bupivacaine in axillary, perivascular brachial plexus block. Can J Anaesth 2001;48:522-5. | 9. 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. | 10. Eledjam JJ, Deschodt J,Viel EJ, Lubrano JF, Charavel P, d'Athis F,et al. Brachial plexus block with bupivacaine: Effects of added alpha-adrenergic agonists: Comparison between clonidine and epinephrine.Can J Anaesth 1991;38:870-5. | 11. Fukuda T, Dohi S, Naito H. Comparisons of tetracaine spinal anesthesia with clonidine or phenylephrine in normotensive and hypertensive humans. Anesth Analg 1994;78:106-11. | 12. Bonnet F, Brun-Buisson V, Saada M, Boico O, Rostaing S, Touboul C. Dose-related prolongation of hyperbaric tetracaine spinal anesthesia by clonidine in humans. Anesth Analg 1989;68:619-22. | 13. Dobrydnjov I,Samarütel J.Enhancement of intrathecal lidocaine by addition of local and systemic clonidine.Acta Anaesthesiol Scand 1999;43:556-62. | 14. Ota K, Namiki A, Ujike Y, Takahashi I. Prolongation of tetracaine spinal anesthesia by oral clonidine.Anesth Analg 1992;75:262-4. | 15. Pertovaara A, Kauppila T, Jyväsjärvi E, Kalso E. Involvement of supraspinal and spinal segmental alpha- 2- adrenergic mechanisms in the medetomidine induced antinociception. Neuroscience 1991;44:705-14. | 16. Samsó E,Vallés J,Pol O,Gallart L,Puig MM. Comparative assessment of the anaesthetic and analgesic effects of intramuscular and epidural clonidine in humans. Can J Anaesth 1996;43:1195-202. | 17. Butterworth JF 5th,Strichartz GR.The alpha 2 adrenergic agonists clonidine and guanfacine produce tonic and phasic block of conduction in rat sciatic nerve fibers.Anesth Analg 1993;76:295-301. | 18. Moss J, Glick D.The Autonomic Nervous System. In Miller RD(ed): Miller's Anesthesia 6th Ed.Philadelphia,PA:Elsevier Churchill Livingstone 2005;650-651. |