

## COMPARISON OF INTRATHECAL BUPIVACAINE WITH OR WITHOUT CLONIDINE FOR PERIOPERATIVE ANALGESIA IN LOWER LIMB ORTHOPEDICS SURGERIES

Dr Rajit Kumar<sup>1</sup>, Dr Shalendra Singh<sup>2</sup>, Dr Sunny Eapen<sup>3</sup>, Dr Raghavendra Kumar Giri<sup>4</sup>, Dr Priya Taank<sup>5</sup>, Dr Munish Sood<sup>6</sup>

<sup>1</sup>MD, Department of Anaesthesia and Critical Care, Command Hospital (AF), Bangalore

<sup>2</sup>DM, Department of Anaesthesia and Critical Care, AFMC, Pune

<sup>3</sup>MD, Department of Anaesthesia and Critical Care, AFMC, Pune

<sup>4</sup>MD, Department of Anaesthesia and Critical Care, Command Hospital (AF), Bangalore

<sup>5</sup>MD, Department of Ophthalmology, AFMC, Pune

<sup>6</sup>DNB, Dept of orthopedics, Command Hospital Chandigarh

**Article Info:** Received 15 August 2019; Accepted 06 September. 2019

**DOI:** <https://doi.org/10.32553/ijmbs.v3i9.520>

**Address for Correspondence:** Dr Sunny Eapen, MD, Department of Anaesthesia and Critical Care, AFMC, Pune-40

**Conflict of interest:** No conflict of interest.

### Abstract

**Background:** The newer adjuncts for spinal anaesthesia (SA) have seen numerous modifications over the last two decades. Various doses of clonidine have been tried in past but optimal dose which balances the ill effects has to be discovered. Therefore, this study was designed to study the effect of clonidine as an adjuvant in SA in terms of duration and complication.

**Methods:** Two groups I and II ( with 60 patients each) received either 3.0 ml of Bupivacaine 0.5% heavy + 0.5 ml of normal saline and 2.5 ml of bupivacaine 0.5% heavy + 0.5 ml (75µg) of preservative free clonidine respectively. Various haemodynamic parameters and complication were recorded at baseline than 30 min, 1,2,4,6 and 8 hours after SA.

**Results:** Group II shows that addition of clonidine had altered the heart rate and blood pressure significantly for initial two hour duration( $p<0.05$ ). No difference in the onset of sensory and motor blockade in both groups. Majority of patients in both group had level of sensory block upto T7 level. Mean VAS score was significantly lower in group II ( $p<0.001$ ). Group II has prolonged duration of motor blockade ( $p<0.001$ ). The difference in mean duration of analgesia among both the groups was significant indicating that addition of clonidine prolongs the duration of analgesia ( $p<0.0001$ ). In group II incidence of hypotension and bradycardia is more as compared to group I.

**Conclusion:** Intrathecal clonidine in the dose of 75 µg along with bupivacaine 0.5% heavy prolonged postoperative analgesia and motor blockade. It produces sedation in which patients were asleep and easily arousal and haemodynamic changes which could be easily managed.

**Keywords:** Intrathecal, Bupivacaine, Clonidine, Orthopedics surgeries, VAS score

### Introduction:

The quest for safer and newer adjuncts for spinal anaesthesia (SA) has seen numerous modifications over the last two decades<sup>1,2</sup>. Till date opioids in 0.5% hyperbaric bupivacaine has been the most commonly used drug in SA. Intrathecal and oral Clonidine, a  $\alpha_2$  adrenergic agonist, has been shown to result in the prolongation of the sensory blockade and the reduction in the amount or the concentration of local anesthetic required to produce post operative analgesia<sup>3</sup>. It also has the ability to prolong the motor blockade produced by bupivacaine. Optimal doses of clonidine as an adjuvant to local anesthetic producing prolonged post operative analgesia and minimal side

effects would be a true alternative to opioids with their dangerous side effects. Therefore, this study was designed to study the effect of clonidine as an adjuvant to bupivacaine heavy, given intrathecally for prolonging the duration of analgesia and to compare the efficacy in terms of duration and complication.

### Materials and method

After approval from the Institutional Ethics Committee, written informed consent was obtained. A total of 120 patients in age group of 20-50 years accepted in American Society of Anaesthesiology Grade I who reported for lower limb orthopedic surgeries, were divided into two groups (odds number were allocated to Group I and even to Group

II) as per simple randomization. Patient with infection of the lower back, coagulopathy or on anticoagulant therapy, any cardiovascular disease, increased intracranial tension or pre-existing neurological disease and severe deformity of spine were excluded from the study. Patients in group "I" (n=60) received 3.0 ml of Bupivacaine 0.5% heavy + 0.5 ml of normal saline and patients in Group II (n=60) received 2.5 ml of bupivacaine 0.5% heavy + 0.5 ml (75µg) of preservative free clonidine. After securing a suitable peripheral vein, all patients were being administered 10ml/kg of lactate ringer's solution as preload. Baseline Heart rate (HR), Systolic blood pressure (SBP), respiratory rate (RR), pulse oximetry (SPO<sub>2</sub>) and electrocardiography (ECG) is to be recorded. Under all aseptic precautions, lumbar puncture is to be performed in L<sub>3</sub>-L<sub>4</sub>, L<sub>2</sub>-L<sub>3</sub> subarachnoid space with patients in sitting position. Onset of action of block, time to reach block, Bromage scale, Visual analogue scale (VAS), state of analgesia and complication was recorded during intraoperative and postoperative period. The patient who required analgesic was be given Inj Diclofenac75mg IM as and when pain occurred. Sensory analgesia was tested by pin prick method. Absence of response to pin prick was taken as onset of sensory analgesia. The time taken from injection of drug to absence of response to pin prick was recorded as time of onset of sensory analgesia. Onset of motor blockade was taken as the time elapsing from injection to failure to raise the lower limb on command. Degree of motor block was assessed by patient's movement of leg, and feet till no further change was observed. This was classified into four grade, according to criteria described by Bromage P.R. (Grade 0 (nil) -free movement of leg and feet, I (partial)- just able to flex knee with free movement of feet, II (almost complete) - unable to flex knee with free movement of feet, III (complete) - unable to move leg and feet. HR, BP and RR were recorded every 5 min till 30<sup>th</sup> min and than half hourly till the completion of surgery. In postoperative period they were recorded in immediate postoperative period and thereafter at different time intervals. HR < 50/min was graded as bradycardia. HR > 120/min was graded as tachycardia. 0.6 mg atropine was kept ready if needed in any episode of bradycardia. If BP fall more a 20% from the base line, it was treated by injection ephedrine. Degree of sedation was closely monitored based on scoring system introduced by Chernik et al (0-Wide awake, 1- Sleeping comfortably

but responding to verbal command, 2-Deep sleep but arousable, 3-deep sleep not arousal).Duration of motor blockade was recorded as time taken from the onset of the motor blockade to the time when the patient was able to move leg. Assessment of pain was done by patients themselves, and for this assessment visual analogue scale (VAS) was used. The top of the scale at 100 represents maximum unbearable pain which the patient can imagine with the baseline 0 represents no pain. The patient was asked to mark on the scale the degree of pain that he was having at that moment. Patients were closely observed postoperatively for 24 hrs to note the complications like nausea, vomiting, drowsiness, dryness of mouth, hypotension, bradycardic, shivering, itching, urinary retention, headache, backache etc.

All the relevant data were recorded in proforma prepared for the study and results thus obtained were subjected to statistical analysis. Data analysis was done by using SPSS. The statistical technique used was one-way analysis of variance (ANOVA) followed by multiple comparisons among groups by Bonferroni method. The comparison over period of time was carried out by using two ways ANOVA (Repeated measure. analysis) along with multiple comparisons by Bonferroni cant group. The significance was observed if  $p < 0.05$ .

## Result

Majority of patients were in age group 31-40 years in both groups. (Table1) Variation from the base line value and the difference in HR and SBP of both the groups during ½ hour to 2 hour duration was statistically significant ( $p < 0.05$ ) The difference in HR and SBP after 2 hour duration was insignificant. (Table 2) It suggests that addition of clonidine had altered the HR and SBP significantly for initial two hour duration and then come to baseline value. Onset of sensory blockade was in the range of 121-180 seconds in majority of patients (n=36, 60%) in group I and (n=40, 66.67%) in group II. The difference in mean onset of analgesia among both the groups was statistically insignificant ( $p > 0.05$ ), indicating that addition of clonidine had not shortened the onset of sensory blockade. Onset of motor blockade was in the range of 241-300 seconds in majority of patients in both groups (n=34, 56.67%) in group I and (n=34, 56.67%) in group II. The difference in mean onset of motor blockade among both the groups was insignificant statistically ( $P > 0.05$ ) indicating that addition of clonidine had not shortened the onset of

motor blockade. All patients had a grade 3 motor blockade in both groups. Level of sensory block obtained in both group were statistically insignificant. Majority of patients in both group had level of sensory block upto T7 level. Level of motor block obtained in both group were statistically insignificant. Better sedation score was obtained by addition of clonidine. Mean VAS score was significantly lower in group II as compared to group I. The difference between the mean VAS score at different time, among both the groups, was statistically significant ( $p < 0.001$ ) (Table 2). In majority of patients in group I ( $n=38, 63.33\%$ ) had duration of motor blockade in the range of 121-180 minutes, while only ( $n=4, 6.67\%$ ) patients in group II had motor blockade within this range. In group II majority of patients had duration of motor blockade in the range of 241-300 (50 %). The difference in the mean duration of motor blockade among both the groups was significant statistically

( $p < 0.001$ ) Duration, of analgesia with Bupivacaine alone was in the range of 150-310 minutes. Duration of analgesia was prolonged by addition of clonidine. Duration of analgesia in group II was in the range of 440-660 minutes. In majority of patients in group 1 it was in the range of 121-240 minutes ( $n=42, 70\%$ ) while in group II, it was in the range of 481-600 minutes in majority of patients ( $n=36, 60.00\%$ ). The difference in mean duration of analgesia among both the groups was statistically significant ( $P < 0.0001$ ).

In group II incidence of hypotension and bradycardia is more as compared to group I. Two patients in group I and three patients in group II had hypotension and bradycardia within 30 min of SA, managed with atropine and mepentermine. In group II, 9 patients had dryness of mouth and none in group I. In both groups 2 patients had shivering intraoperatively. In Group I all the patients were having sedation score of 0.

**Table 1: Demographic profile and clinical characteristics of the patients**

Patient data	Group I (n=60) mean $\pm$ SD	Group II (n=60) mean $\pm$ SD	P value
Age(yrs)	34.4 $\pm$ 7.5	35.3 $\pm$ 7.4	0.50
Onset of sensory blockade	181.7 $\pm$ 37.3	172.3 $\pm$ 37.2	0.16
Onset of motor blockade	302 $\pm$ 57.9	288.3 $\pm$ 53.8	0.18
Duration of analgesia	219 $\pm$ 38.4	574 $\pm$ 63.1	0.0001
Duration of motor blockade	167.5 $\pm$ 23.4	244 $\pm$ 32.5	0.0001
RR (/min)	16 $\pm$ 0.8	16.4 $\pm$ 0.9	0.01
Duration of surgery	76.4 $\pm$ 16.5	77.6 $\pm$ 17.4	0.69

#HR-Heart rate,RR-Respiratory rate

**Table 2: Systemic hemodynamic parameters at different time interval (values expressed as mean  $\pm$  SD or number) during observation period in two groups**

value		Preop	30 min	1 hrs	2 hrs	4 hrs	6 hrs	8 hrs
HR	Group I	84.67 $\pm$ 9.45	83.4 $\pm$ 9.4	84.8 $\pm$ 6.3	84.5 $\pm$ 6.3	83.6 $\pm$ 7.2	83.9 $\pm$ 7	84.5 $\pm$ 6.4
	Group II	83.86 $\pm$ 9.42	69.7 $\pm$ 7.6	72 $\pm$ 7.2	79.8 $\pm$ 8.2	81.3 $\pm$ 8.4	81.6 $\pm$ 7.9	82.7 $\pm$ 7.3
SBP	Group I	126.67 $\pm$ 12.13	114. $\pm$ 11.80	117.33 $\pm$ 11.46	120.33 $\pm$ 9.99	121.33 $\pm$ 8.19	123.33 $\pm$ 8.44	124.66 $\pm$ 8.99
	Group II	125 $\pm$ 12.52	107.4 $\pm$ 10.63	109.66 $\pm$ 10.25	110.33 $\pm$ 9.44	115.67 $\pm$ 7.74	118.33 $\pm$ 9.49	122.66 $\pm$ 8.69
VAS Score	Group I	-	-	-	15.83 $\pm$ 5.58	47.83 $\pm$ 6.61	73 $\pm$ 7.83	83.86 $\pm$ 5.45
	Group II	-	-	-	0 $\pm$ 0	1.67 $\pm$ 2.50	7.167 $\pm$ 8.97	18.83 $\pm$ 16.01

#HR-Heart rate, SBP-Systolic blood pressure,VAS- Visual analogue score

**Discussion**

The dose of intrathecal clonidine has been selected based on previous literature available. The search revealed that different studies have been done with different doses of clonidine ranging from 20 $\mu$ g to 150 $\mu$ g. It is found that higher dose of clonidine (2 $\mu$ g/kg body weight) significantly prolongs the analgesia but causes higher incidence of hypotension and bradycardia. Addition of lesser

doses than 75  $\mu$ g clonidine produced high quality anaesthesia but did not significantly prolonged sensory or motor blockade. Dose selection of 75  $\mu$ g in our study was based on the selected by most of previous worker. All patients were given SA by a blind technique, however newer ultrasound guided technique found to favorable to give SA but it requires technical expertise<sup>4</sup>.

In our study no difference in the onset of sensory and motor blockade in clonidine group. In a study conducted by Grandhe PR et al.<sup>5</sup> authors observed onset of analgesia to be  $7.6 \pm 2.2$  mins in control group (7.5mg of hyperbaric bupivacaine) and it was  $7.1 \pm 4.2$  mins and  $8.2 \pm 3.4$  mins in clonidine group (clonidine 1  $\mu\text{g}/\text{kg}$  and 1.5  $\mu\text{g}/\text{kg}$  respectively) which is more than the value in our study. This could be due to the less mass of hyperbaric bupivacaine (7.5mg) used and patients were kept in the lateral position for 15 min after the administration of the drug and authors have not mentioned whether they have noted the onset of analgesia on the dependant side or on the non dependant side. Maximum level of sensory blockade achieved in both the groups was between T7 and T9. In a study conducted by Saxena H et al.<sup>6</sup> there was no statistically significant difference in the maximum level of sensory blockade and this probably may be due to large mass of hyperbaric bupivacaine (13.5mg) used. Our study concurs with the study conducted by Strebel S et al.<sup>7</sup> who observed the mean duration of analgesia to be  $381 \pm 117$  mins when using clonidine of 75  $\mu\text{g}$  and Grandhe PR et al.<sup>5</sup> observed the mean duration of analgesia of  $6.3 \pm 0.8$  hours when using clonidine of 1  $\mu\text{g}/\text{kg}$  with a mean weight of  $60.6 \pm 19.4$  kg. In a study conducted by van Tuijl I et al.<sup>8</sup> authors observed the duration of analgesia to be 55 mins in control group (2.2ml bupivacaine, 0.5%, heavy) and 129 mins in clonidine group.

The mechanism of clonidine induced potentiating of sensory block in spinal anaesthesia is reported to be mediated by presynaptic (inhibition of transmitter release) and post synaptic (enhancing hyperpolarisation) affects. In our study duration of motor blockade is taken as the time required for recovery of complete power of lower limbs (Bromage grade 0) from the time of induction of spinal anaesthesia. In our study the mean duration of motor blockade was  $167.5 \pm 23.44$  minutes in control group and  $244 \pm 32.55$  minutes in clonidine group, which is statistically highly significant.

### Conclusion

From our study, we conclude that intrathecal clonidine in the dose of 75  $\mu\text{g}$  along with 3 ml

bupivacaine 0.5% heavy in patients undergoing lower limb orthopedic surgeries prolonged postoperative analgesia and motor blockade. It produces sedation in which patients were asleep and easily aroused and haemodynamic changes which could be easily managed. It was not associated with side effects like pruritus and respiratory depression and hence can be an attractive alternative for opioids for prolonging spinal analgesia.

Conflict of interest: Nil

### References

1. Goel N, Singh S, Kumar Prasantha HM, Jain A, Singh A. Comparison of intrathecal levobupivacaine with fentanyl and bupivacaine with fentanyl in cesarean section. *Global Journal of Research Analysis* 2019; 8(4):68-70.
2. Bhatia P, Singh S, Trivedi S, Dwivedi D. Compare the efficacy of butorphanol with conventional opioids in patients undergoing spinal surgeries under general anaesthesia. *Global journal for research analysis* 2019; 8(7): 27-29.
3. Mohanty A, Singh S, Sinha JK, Sharma R, Taank T. Clinical analysis of oral clonidine and intramuscular pethidine with glycopyrrolate as premedication in patient under general anaesthesia. *International Journal of Biomedical Research* 2019; 10(04):e5119.
4. Bal A C, Singh S, Eapen S, Gupta A, Taank P. To study efficacy of ultrasound guided paramedian technique in administering spinal anaesthesia. *International Journal of Medical and Health Research* 2019; 5 (8): 128-30.
5. Grandhe PR, Wig J, Yaddanapudi LN. Evaluation of bupivacaine-clonidine combination for unilateral spinal anaesthesia in lower limb orthopedic surgery. *J Anaesth Clin Pharmacol* 2008; 24(2):155-8.
6. Saxena H, Singh SK, Ghildiyal S. Low dose intrathecal clonidine with bupivacaine improves onset and duration of block with haemodynamic stability. *The internet journal of Anaesthesiology* 2010; 23:1.
7. Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH. Small dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery. A dose response study. *Anesth Analg* 2004; 99:1231-8.
8. Van Tuijl I, Van Klei WA, Van der Werff DBM, Kalkman CJ. The effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements after cesarean section: a randomized controlled trial. *British Journal of Anaesthesia* 2006; 97(3):365-70.