

INTRATHECAL USE OF CLONIDINE WITH HYPERBARIC BUPIVACAINE IN ORTHOPAEDIC SURGERIES OF LOWER LIMBChandrashekharappa K¹, Ravindra C. G², Kumara A. B³, Kiran M⁴**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: BACKGROUND: Clonidine, an α_2 adrenergic agonist is used as adjuvant to local anesthetics with variable results. We studied effects of the intrathecal use of low dose clonidine with 0.5% hyperbaric bupivacaine on duration of analgesia and hemodynamic parameters. **METHOD:** This prospective study done on 60 patients belonging to ASA 1 or 2, undergoing orthopedic surgeries of lower limb under subarachnoid block were randomized into two groups(30 patients each), group 1 received saline and group 2 received 30 μ g clonidine as adjuvant along with 2.5 ml of 0.5% hyperbaric bupivacaine intrathecal injection. During study, the duration and onset of sensory and motor block, duration of analgesia, and total requirement of rescue analgesics along with hemodynamic changes and side effects of study drugs were recorded. **RESULTS:** we found time delay in onset of both sensory and motor block in clonidine group which was statistically insignificant, and significant prolongation of both sensory (140.26 minutes Vs. 93.63 minutes) and motor blockade (153.74 minutes Vs. 104.79 minutes) p-value <0.001. **CONCLUSION:** Adjuvant use of low dose clonidine (30 μ g) with hyperbaric bupivacaine prolongs the duration of both sensory and motor blockade, and duration of analgesia without much hemodynamic adverse effects.

KEYWORDS: Intrathecal clonidine, hyperbaric bupivacaine, lower limb surgeries, α_2 adrenergic agonist.

INTRODUCTION: Lower limb orthopedic surgeries are preferably done under central neuraxial blockade mainly sub-arachnoid block for short duration surgeries. Bupivacaine is the standard local anesthetic for sub-arachnoid block for these surgeries. For prolongation of regional anesthesia, adjuvants are added to local anesthetics like opioids, α_2 agonists, epinephrine etc.

Clonidine is a frequently used adjuvant to local anesthetics (LA). The analgesic properties of clonidine when administered intrathecally or epidurally have been demonstrated; Moreover, others have indicated an increased incidence of adverse effects like sedation, hypotension and bradycardia.¹⁻³

Clonidine has been shown to be of benefit for use in central neuraxial blocks and other regional blocks by increasing the duration and intensity of pain relief^{4,5} as also by decreasing the systemic and local inflammatory stress response.⁶⁻⁸

So, we decided to study Intrathecal effects of clonidine with hyperbaric bupivacaine in patients undergoing lower limb orthopedic surgeries.

METHODS: After institutional approval and informed written consent, a prospective randomized study was conducted on 60 adult patients undergoing lower limb orthopedic surgeries. Patients aged between 18 to 70 years, of either gender, height of 150 to 170 cms, ASA physical status 1 or 2 were included in our study and were divided into two groups, group 1: bupivacaine with saline (BS) and

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group 2: bupivacaine with clonidine (BC). Patients excluded are those with contra-indications for subarachnoid block, patients with significant neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal or hepatic disease or alcohol or drug abuse, and pregnant or lactating women. Patients taking medications with psychotropic or adrenergic activities and patients receiving chronic analgesic therapy were also barred from the study.

All patients were evaluated in the pre-anesthetic clinic. Any specific investigations, if required according to the individual cases were also done. Patients were familiarized with visual analogue scale (VAS)⁹ and its use for measuring the postoperative pain. All patients were fasted overnight for 8 to 10 hrs. and received Tab Alprazolam 0.5 mg as premedication a night before and 0.25 mg in morning on the day of the surgery.

Intraoperative: In the operation theatre all patients were again explained about the procedure and use of VAS; and electrocardiogram (ECG), pulse oximetry, and non-invasive blood pressure were attached and baseline parameters were recorded and monitoring was initiated. Intravenous (IV) access was secured and all patients were preloaded with ringer lactate 10 ml/kg. Patients were randomly assigned using sealed envelope technique into two groups BS and group BC.

Under strict aseptic precautions, patient in sitting position, lumbar puncture was performed with the patient in the sitting position at the L₃₋₄ or L₂₋₃ interspace, with a 24-gauge Quincke-point needle. Group BS were injected with 12.5 mg 0.5% hyperbaric bupivacaine with 0.2 mL of normal saline and group BC injected with 12.5 mg of 0.5% hyperbaric bupivacaine with 30 µg (0.2 mL) of clonidine after ensuring free flow of clear CSF.

The following parameters were assessed and compared:

- Time for onset of sensory block and adequate level of analgesia (T10, assessed with pinprick).
- Time for onset of motor block assessed by modified Bromage scale.¹⁰
- Peak sensory level reached (assessed with pinprick)
- Time at two segment regression from peak level of sensory block.
- Time for motor block to recede to L 3-4 level, ability to flex knee
- Duration of sensory block.
- Incidence of complications including –respiratory depression, hypotension, bradycardia, nausea and vomiting, sedation, shivering and mandatory bladder catheterization within 12 hours.

0	No sedation (awake and alert)
1	Drowsy
2	Asleep, responding to verbal commands
3	Asleep, not responding to verbal commands
Sedation scale	

The cephalad spread of analgesia and the degree of motor blockade of the lower limbs was recorded every 5 minutes. The level of sensory blockade was assessed using a 25 gauge short bevel needle and recorded as analgesia to loss of sensation to pin prick. Motor blockade was determined according to the modified Bromage score¹⁰

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- 0 - No paresis - the patient is able to move the hip, knee, and ankle;
- 1 - Partial paresis - the patient is unable to move the hip, but is able to move the knee and ankle;
- 2 - Partial paresis - the patient is unable to move hip and knee, but is able to move the ankle;
- 3 - Complete paresis – the patient is unable to move the hip, knee, and ankle.

Complete motor block recovery was assumed when modified Bromage score was 3.

The parameters such as heart rate, non-invasive blood pressure, ECG and SpO₂ were periodically monitored and recorded at 5 minutes interval. A note was also made of blood loss, urine output, IV fluid input. Patients were observed for any discomfort, nausea, vomiting, shivering, pain, bradycardia and any other side effect and the need for additional medications was recorded.

IV fluid was administered in the form of Ringer's lactate, in calculated doses depending on the weight of the patient and further adjusted as per blood loss during surgery. A fall of systolic arterial blood pressure (SBP) to less than 90 mm of Hg or fall below 30% of baseline value was treated with rapid infusion of 500 ml of RL and 3 mg aliquots of injection mephentermine intravenously if there was no response to fluid administration. Bradycardia (heart rate less than 50/minute) was treated with intravenous atropine sulphate (0.6 mg). For patients with shivering, cotton roll and blankets were used.

All patients were observed in the post-anesthesia recovery room and then in the ward. Severity of pain was measured using a 10 cm visual analogue scale (VAS) at 0, ½, 1, 2, 4, 6, 12 and 24 hour intervals for next 24 hours by the nursing staff. If patient has VAS of >3 or complains of pain with VAS >3 were given rescue analgesia by injection Diclofenac sodium 75 mg intramuscularly. The time of onset of pain was recorded and frequency of rescue analgesia required in each case was recorded.

The various data obtained, which included the hemodynamic parameters, respiratory rate, SpO₂, duration of analgesia were calculated and compared with baseline values within each group as well as with corresponding times among the groups, using paired t-test and students t-test respectively. A 'P' value <0.05 was taken as significant.

RESULTS: Both the groups were comparable in terms of age, gender, height and weight (Table 1). Table 2 shows the number of patients in two groups undergoing different types of lower limb surgeries. The duration of surgery between the groups was almost similar according to the type of procedure performed and clinically comparable.

	Group BS	Group BC	p - value
Age in years	53.8 ± 18.64	52.7 ± 15.85	0.8064
Gender – male: female	17:13	20:10	0.4257
ASA physical status (1 or 2)	14:16	12:18	0.6023
Height in centimetres	156.8±5.4	160.6±6.6	0.01773
Weight in kilograms	60.6±10.8	58.8±12.6	0.5548
Duration of surgery in minutes	112.2±24.4	106.8±32.2	0.4671

Table 1: Demographic Profile

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Type of lower limb surgeries	Group BS			Group BC		
	MALE	FEMALE	Total	MALE	FEMALE	Total
1. Dynamic Hip Screw fixation	5	3	8	4	4	8
2. Fracture Tibia for OR+IF	2	1	3	2	1	3
3. Fracture Shaft of femur OR+IF	5	4	9	5	2	7
4. Tension Banding Wiring of patella fracture	1	0	1	5	0	5
5. Bi/Tri-Malleolar fracture of ankle	1	1	2	4	2	6
6. Fracture neck of Femur- Austin Moore Prosthesis	3	4	7	0	1	1
TOTAL	17	13	30	20	10	30

Table 2: Type of lower limb surgeries

Adverse events	Group BS	Group BC
Bradycardia	0	2 (6.67%)
Hypotension	1 (3.33%)	2 (6.67%)
Nausea/ vomiting	0	1 (3.33%)
Sedation score: 2 or more	0	1 (3.33%)
Shivering	1 (3.33%)	0

Table 3: Adverse events

In group BC, the onset of sensory block was slower compared to the group BS. The onset of sensory block was defined as the time between injection of intrathecal anesthetic and the absence of pain at the T12 dermatome assessed by sterile pinprick every 2 min till T10 dermatome was achieved. The onset of motor block was also delayed in group BC compared to group BS, but onset of both sensory and motor block between groups were statistically insignificant.

The mean duration of analgesia was 140.26 minutes in group BC compared to 93.63 minutes in group BS. Similarly, mean duration of motor block was 153.74 minutes in group BC compared to 104.79 minutes in group BS. The duration of sensory block and motor block was prolonged in group BC compared to group BS, which was both clinically and statistically significant ($p < 0.001$).

On overall the duration of spinal anesthesia was prolonged in patients who received intrathecal clonidine with bupivacaine. The total number of Diclofenac injections received over 24 hour post operatively was significantly lower in clonidine group compared to saline group.

The blood pressure were comparable between the groups with one patient having hypotension in group BS compared to two patients in group BC, but in rest of the patients of group BC had comparable values as group BS. Two patients in group BC had bradycardia requiring treatment with injection atropine. There was no significant change in respiratory rate and SpO₂ from the baseline values in both the groups.

None of the patients experienced respiratory distress at any point of time. All patients had peripheral oxygen saturation (SpO₂) greater than 96% at all the times and did not require additional

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oxygen in PACU. One patient in group BC had nausea and was treated with intravenous injection of Ondansetron 4 mg. In group BS, one patient had shivering intraoperatively as compared to none of the patients in group BC.

Characteristics	Group BS		Group BC		p-value	significance
	Mean	Standard Deviation	Mean	Standard Deviation		
Time of onset of sensory block	3.99	0.95	4.12	0.63	0.515	Not significant
Time of onset of motor block	4.60	0.98	4.77	0.63	0.435	Not significant
Time of sensory block for 2 segment regression	93.63	12.19	140.26	16.29	<0.001	Significant
Time of regression of motor block	104.79	13.77	153.74	16.71	<0.001	Significant
Time of first rescue analgesic given	102.19	13.23	169.57	18.12	<0.001	Significant

Table 4: Characteristics of subarachnoid block

DISCUSSION: Clonidine, a selective partial agonist at α_2 adrenergic receptors is known to produce analgesia after intrathecal administration mediated through activation of post synaptic α_2 receptors in substantia gelatinosa of spinal cord. When used as an adjuvant to local anesthetics it is known to prolong both sensory and motor blockade, but dose at which it produced above effect in previous studies have been known to produce side effects like hypotension, bradycardia and sedation.^{11, 12}

Total duration of sensory block in our study was 140.26 minutes which is in accordance with study by Hema Saxena et al¹³ and was less compared to study by Ramila R Jamliya et al,¹⁴ may be due to the dose of bupivacaine used in our study (12.5 mg) but in terms of prolongation of duration of sensory block was in accordance with above studies.

Clonidine group in our study had delayed onset of both sensory and motor block which was not statistically significant compared to the study by Gandhe et al¹⁵ and Ramila R Jamliya et al¹⁴ who had similar result but significant statistically.

I. Van Tuijl et al¹⁶ studied use of clonidine 75 μ g with hyperbaric bupivacaine in 53 pregnant patients, and found 58% of the study group patients had hypotension compared to 6% to 7% of patients in our study probably due to use of 75 μ g clonidine in their study (comparison to 30 μ g). Even though they have used 11 mg of hyperbaric bupivacaine in their study compared to 12.5 mg bupivacaine in our study.

Even though, incidence of hypotension and bradycardia were present in clonidine group, other side effects of intrathecal clonidine was comparable to other previous studies; one of patient had sedation which was not significant, similar to study by I. van Tuijl et al¹⁶ but was significant in study by B.S. Sethi et al¹², and similar to these earlier studies, no patient had incidence of respiratory depression.

One patient in control group had shivering compared to none in study group was not significant. One patient in clonidine group had nausea requiring treatment probably due to hypotension in the same patient. None of patient had urinary retention similar to previous studies.

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In consistent with most of studies on intrathecal use of clonidine with hyperbaric bupivacaine, B.S.Sethi et al,¹² Saxena et al,¹³ Kaabachi et al,¹⁷ Elia et al,¹⁸ Cao JP,¹⁹ our study showed prolongation of analgesia and significantly less requirement of rescue analgesics over 24 hour study period at 30 µg of clonidine in comparison to much higher doses of intrathecal clonidine in previous studies, significantly reducing hemodynamic side effects. Using clonidine in place of opioids avoids side effects related to them like pruritus, urinary retention and respiratory depression.

We conclude that addition of 30 µg of clonidine to 0.5% hyperbaric bupivacaine intrathecally can prolong the sensory and motor blockade, and duration of analgesia without much hemodynamic adverse effects.

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