

# Evaluation of bupivacaine-clonidine combination for unilateral spinal anesthesia in lower limb below-knee orthopedic surgery

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## ABSTRACT

**Background and Objectives:** The purposes of this study were to evaluate the onset, quality and duration of sensory and motor blockade between hyperbaric bupivacaine and clonidine combination with bupivacaine alone when administered intrathecally for unilateral spinal anesthesia in below-knee orthopedic surgery, efficacy of clonidine for post-operative analgesia and side-effects of clonidine, if any. **Methods:** Sixty ASA I and ASA II patients scheduled for elective surgery with time duration up to 90 min were studied. Patients were randomised in two equal groups by the lottery method. Group A (control group) was given Inj. bupivacaine (hyperbaric) 0.5% - 12.5 mg (2.5 ml) + 0.5 ml of normal saline intrathecally. Group B (clonidine group) was given Inj. bupivacaine (hyperbaric) 0.5% - 12.5 mg (2.5 ml) + 50 mcg clonidine in 0.5 ml volume intrathecally. **Results:** The mean peak sensory block was earlier in Group B (4.7±1.23 min) as compared with Group A (6.27±1.51 min). The mean peak motor block was earlier in Group B (6.17±1.20 min) as compared with Group A (8.63±1.71 min). The two-segment regression of sensory block was longer in Group B (106.23±9.17 min) as compared with Group A (104.43±17.75 min), which is clinically significant. Requirement of rescue analgesia was considerably prolonged in Group B (450.33±95.10 min) as compared with Group A (220±36.36 min), which was also clinically highly significant. **Conclusion:** Intrathecal clonidine potentiates bupivacaine induced spinal sensory block and, motor block and reduces the analgesic requirement in the early post-operative period in unilateral spinal anesthesia for lower limb below knee surgery.

**Key words:** Below-knee surgery, bupivacaine, clonidine, intrathecal

## INTRODUCTION

In lower limb surgical procedures, the regional anesthesia technique has gained popularity because of the absence of biochemical and metabolic changes consequent to the stress of general anesthesia for surgery. Introduction of cocaine (Karl Koller 1884) as a local anesthetic was a stepping stone in the development of spinal analgesia.<sup>[1]</sup>

Spinal anesthesia with bupivacaine is administered routinely for lower limb surgeries. The ensuring nerve block is

sufficient to ensure painless surgery to the patient, while motor block facilitates the surgeons' work. To prolong the duration of spinal anesthesia, a number of adjuvants have been added to local anesthesia, but these are associated with side-effects.

Spinal anesthesia can be prolonged in many ways, i.e., by using adjuvant like adrenaline, opioids, midazolam, neostigmine, etc., to the local anesthetic. Clonidine, either intrathecal or orally, can prolong spinal anesthesia and is free of the opioid-related side-effects. Clonidine hydrochloride, an imidazoline derivative, is a centrally acting  $\alpha_2$  adrenergic agonist and was introduced more than two decades ago as an antihypertensive agent.

The present study was undertaken to evaluate the effects of intrathecal clonidine when administered together with hyperbaric bupivacaine 0.5% in unilateral spinal anesthesia for lower limb below-knee orthopedic surgery.

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**METHODS**

With the approval of the institutional ethical committee, 60 ASA I and ASA II patients of the age group of 18-55 years undergoing elective surgery with time duration up to 90 min were studied. Patients were randomised into two equal groups of 30 patients each by the lottery method.

Group A: Patients were given Inj. bupivacaine (hyperbaric) 0.5% - 12.5 mg (2.5 ml) + 0.5 ml of normal saline intrathecally.

Group B: Patients were given Inj. bupivacaine (hyperbaric) 0.5% - 12.5 mg (2.5 ml) + 50 mcg clonidine in 0.5 ml volume intrathecally.

Patients were kept nil orally for 68 h prior to surgery. Sedatives and hypnotics were avoided in pre-medications as well as intraoperatively.

Spinal anesthesia was given in a sitting position. Depending upon the groups, the respective agents were given intrathecally. After this, the patient was made to lie down in the lateral position for 10 min. The lateral position, right or left, was given with the operative side downwards planned for surgery.

Pulse rate, blood pressure, respiratory rate and oxygen saturation were noted every 5 min for the first 30 min and then, thereafter every 15 min for the next 30 min, at the end of surgery and post-operatively at two segment regressions of sensory block.

Sensory block was tested by pinprick at the left mid-clavicular line till the block reached the T10 level and then surgical incision was allowed. The degree of motor blockade was assessed using the modified Bromage scale [Table 1].

The following observations were made:

- T0 - Time of spinal anesthesia.
- T1 - Time of onset of sensory block.
- T2 - Time of onset of motor block.
- T3 - Time of peak sensory block.
- T4 - Time of peak motor block.
- T5 - Time of two-segment regression of sensory block.
- T6 - Time to first dose of post-operative rescue analgesia.

The two-segment regressions were noted. Post-operative analgesic drugs were given when the patient's VAS score reached >7 (this time it was taken as the time of wear-off of analgesia). Inj. diclofenac 75 mg was given intramuscularly as rescue analgesia.

Patients were assessed for quality of sedation and scoring was performed using the Campbell score [Table 2].

Any side-effects such as hypotension, bradycardia, shivering and hypoxia were noted and treated with appropriate drugs.

The VAS score was calculated [Table 3]. "0" mark means "no pain" at all while "10" represents the "worst pain" he/she had ever felt. Patients rated the degree of pain by making a mark on the scale. Thus, the pain score was obtained by measuring the distance from the "0" end to the indicated mark.

At the end of the study, the results in the two groups were tabulated and statistically analyzed using SPSS software version 10 by the *t*-test.

**RESULTS**

Onset of sensory block was earlier in the clonidine group (49±9.65 s) as compared with the control group (76.67±16.51 s). Onset of motor block was earlier in the clonidine group (71.83±10.29 s) as compared with the control group (86.7±14.41 s). The difference was insignificant, both statistically and clinically.

The peak sensory block [Table 4] was earlier in the clonidine group (4.7±1.32 min) as compared with the control group (6.27±1.51 min). The peak motor block [Table 5] was also faster in the clonidine group (6.17±1.2 min) as compared with the control group (8.63±1.71 min), and this was statistically significant.

Time for two-segment regression of sensory level [Table 6] was prolonged in the clonidine group (116.23±9.17 min)

**Table 1: Modified Bromage scale**

Score	Criteria
1	Complete block (unable to move feet or knee)
2	Almost complete block (able to move feet only)
3	Partial block (just able to move knees)
4	Detectable weakness of hip flexion while supine (full flexion of knees)
5	No detectable weakness of hip flexion while supine
6	Able to perform partial knee bend

**Table 2: Campbell score**

Score	Criteria
1	Wide awake
2	Awake and comfortable
3	Drowsy and difficult to arouse
4	Not arousable

**Table 3: 0-10 VAS Numeric Pain Distress Scale**

No pain		Moderate pain					Unbearable pain				
0	1	2	3	4	5	6	7	8	9	10	

as compared with the control group ( $104.43 \pm 17.75$  min). The duration of analgesia [Table 7] in the clonidine group ( $450.33 \pm 95.10$  min) was significantly prolonged as compared with the control group ( $220 \pm 36.36$  min), and this was statistically significant.

The mean heart rate in the clonidine group, pre-operatively, was  $83.13 \pm 10.93$  min. It declined after 10 min to  $71.63 \pm 9.93$  min, and remained almost same thereafter. At the end of the surgery, it was  $73.37 \pm 8.07$  min. The mean heart rate in the two groups was compared by applying the unpaired *t*-test at various time intervals, and this showed a statistically significant difference between the two groups after 10 min.

The mean systolic and diastolic blood pressures in the two groups was compared at various time intervals, and showed no statistically significant difference in the two groups.

In the present study, sedation was higher in patients in the clonidine group (12 patients) as compared with patients in the control group, where no patient was sedated.

**Table 4: Comparison of peak sensory block**

Parameter	Group A mean $\pm$ SD (n=30)	Group B mean $\pm$ SD (n=30)	F value	P value
Peak sensory block (T <sub>3</sub> ) (minutes)	6.27 $\pm$ 1.51	4.7 $\pm$ 1.23	4.288	0.000

**Table 5: Comparison of onset of peak motor block**

Parameter	Group A mean $\pm$ SD (n=30)	Group B mean $\pm$ SD (n=30)	F value	P value
Peak motor block (T <sub>4</sub> ) (minutes)	8.63 $\pm$ 1.71	6.17 $\pm$ 1.20	6.424	0.000

**Table 6: Comparison of two-segment regressions of sensory block**

Parameter	Group A mean $\pm$ SD (n=30)	Group B mean $\pm$ SD (n=30)	F value	P value
Two-segment regression (T <sub>5</sub> ) (in minutes)	104.43 $\pm$ 17.75	106.23 $\pm$ 9.17	3.235	0.002

**Table 7: Comparison of time for requirement of rescue analgesia (duration of effective analgesia)**

Parameter	Group A mean $\pm$ SD (n=30)	Group B mean $\pm$ SD (n=30)	F value	P value
Rescue analgesia (T <sub>6</sub> ) (in minutes)	220 $\pm$ 36.36	450.33 $\pm$ 95.10	12.391	0.000

In the control group, there was no bradycardia in any patient as compared with the clonidine group, in which one patient had bradycardia that required intervention.

## DISCUSSION

Intrathecal  $\alpha_2$ -agonists are used as adjuvant drugs to local anesthetics.<sup>[2-4]</sup> They potentiate the effect of local anesthetics and allow a decrease in the required doses.<sup>[3,5]</sup> Clonidine is a partial  $\alpha_2$ -adrenoceptor agonist used intrathecally, and has a well-established record of efficacy and safety.<sup>[6]</sup> Its addition to local anesthetics prolongs the duration of both motor and sensory spinal blockade.<sup>[2-4]</sup>

The mechanisms by which intrathecal  $\alpha_2$ -adrenoceptor agonists prolong the motor and sensory block of local anesthetics is not well understood. It is not a result of altered systemic absorption, as the plasma level of bupivacaine was not altered after the addition of intrathecal clonidine to bupivacaine spinal injection.<sup>[7]</sup> It may be an additive or synergistic effect secondary to the different mechanisms of action of the local anesthetic and the  $\alpha_2$ -adrenoceptor agonist.

The local anesthetic acts by blocking sodium channels, whereas the  $\alpha_2$ -adrenoceptor agonist acts by binding to the pre-synaptic C fibers and the post-synaptic dorsal horn neurons. Intrathecal  $\alpha_2$ -adrenoceptor agonists produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons.<sup>[8-12]</sup> This anti-nociceptive effect may explain the prolongation of the sensory block when added to spinal anesthetics.

On the other hand, Yaksh<sup>[13]</sup> has shown that intrathecal  $\alpha_2$ -adrenoceptor agonists can cause a dose-dependent decrease in motor strength in animals. The prolongation of the motor block of spinal anesthetics may result from the binding of  $\alpha_2$ -adrenoceptor agonists to motor neurons in the dorsal horn.<sup>[14]</sup> Most of the clinical experience gained in the use of intrathecal  $\alpha_2$ -adrenoceptor agonists has been described with clonidine. The use of intrathecal clonidine has a well-established synergistic effect with local anesthetics.<sup>[2-5]</sup>

Clonidine is now an acceptable adjuvant to local anesthetics for the epidural route. Clinical trials provide evidence that less clonidine is needed intrathecally than epidurally to produce a nearly similar analgesic effect with fewer side-effects. The rationale behind the intrathecal administration of clonidine is to achieve a high drug concentration in the vicinity of  $\alpha_2$ -adrenoreceptors in the spinal cord. Clonidine produces analgesia at the spinal and supra-spinal sites. The other benefits are antiemetic effect, reduced post-spinal shivering, anxiolysis and sedation.

## CONCLUSION

Thus, it is concluded that a combination of 0.5% hyperbaric bupivacaine 12.5 mg (2.5 ml) with clonidine 50 mcg for producing unilateral spinal anesthesia for lower limb below-knee surgery of medium duration (<90 min) prolongs the sensory and motor block along with significantly longer-lasting post-operative analgesia without any clinically significant adverse effects.

## REFERENCES

- Atkinson RS, Rushman GB, Davier NJ. Spinal analgesia: Intrathecal and Extradural. Lee's Synopsis of Anaesthesia. Oxford: Butterworth Heinemann; 1998. p. 691-716.
- Strebel S, Gurzeler J, Schneider M, Aeschbach A, Kindler C. Small-dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: A dose-response-study. *Anesth Analg* 2004;99:1231-8.
- Dobrydnjov I, Axelsson K, Thörn SE, Matthiesen P, Klockhoff H, Holmström B, *et al.* Clonidine combined with small-dose bupivacaine during spinal anaesthesia for inguinal herniorrhaphy: A randomized double-blinded study. *Anesth Analg* 2003;96:1496-503.
- Dobrydnjov I, Axelsson K, Samarutel J, Holmstrom B. Postoperative pain relief following intrathecal bupivacaine combined with intrathecal or oral clonidine. *Acta Anaesthesiol Scand* 2002;46:806-14.
- De Kock M, Gautier P, Fanard L, Hody J, Lavand'homme P. Intrathecal ropivacaine and clonidine for ambulatory knee arthroscopy. *Anesthesiology* 2001;94:574-8.
- Gordh T Jr, Post C, Olsson Y. Evaluation of the toxicity of subarachnoid clonidine, guanfacine, and a substance P-antagonist on rat spinal cord and nerve roots: Light and electron microscopic observations after chronic intrathecal administration. *Anesth Analg* 1986;65:1303-11.
- Bioco O, Bonnet F, Mazoit JX. Effects of epinephrine and clonidine on plasma concentrations of spinal bupivacaine. *Acta Anaesthesiol Scand* 1992;36:684-8.
- Eisanach JC, De Kock M, Klimscha W. A2 adrenergic agonists for regional anesthesia. *Anesthesiology* 1996;85:655-74.
- Lawhead RG, Blaxall HS, Bylund BD. Alpha-2A is the predominant a-2 adrenergic receptor subtype in human spinal cord. *Anesthesiology* 1992;77:983-91.
- Smith MS, Schambra UB, Wilson KH, Page SO, Hulette C, Light AR, *et al.* Alpha 2 adrenergic receptor in human spinal cord: Specific localized expression of mRNA encoding alpha-2 adrenergic receptor subtypes at four distinct levels. *Brain Res* 1995;34:109-17.
- Yaksh TL, Jage J, Takano Y. *Pharmacokinetics and pharmacodynamics of medullar agents. The spinal actions of a-2 adrenergic agonists as analgesics.* In: Atikenhead, AR, Benad, G, Brown, BR, Baillieres Clinical Anaesthesiology. Vol. 7, No. 3. London: Bailliere Tindall; 1993. p. 597-614.
- Fairbanke CA, Wilcox GL. Spinal antinociceptive synergism between morphine and clonidine persists in mice made acutely or chronically tolerant to morphine. *J Pharmacol Exp Ther* 1999;288:1107-16.
- Yaksh TL. Pharmacology of spinal adrenergic systems which modulate spinal nociceptive processing. *Pharmacol Biochem Behav* 1985;22:845-58.
- Smith C, Birnbaum G, Carter JL, Greenstein J, Lublin FD. Tizanidine treatment of spasticity caused by multiple sclerosis. *Neurology* 1994;44:34-43.

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