

# Low Dose Intrathecal Clonidine Enhances the Effects of Ropivacaine and Improved the Quality of Recovery after Ambulatory Anorectal Surgery

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## ABSTRACT

**Background:** The aim of this prospective, randomised double-blinded study was to explore the effects of clonidine with ropivacaine in intrathecal anesthesia, concerning the onset and regression of sensory and motor blockade and analgesic effects and improved the quality of recovery after ambulatory anorectal surgery.

**Methods:** We randomly selected 120 patients from the ASA grade I-III; these patients were scheduled for elective anorectal surgery. These patients were randomly select for two groups (n=60 in each group). In the group I: 0.75% ropivacaine (1ml) with isotonic saline and group II 0.75% ropivacaine (1ml) with 30 µg clonidine. An oral 7.5 mg midazolam premedication was given 2 hours preoperatively. Ringer's lactate hydration solution (15ml/kg body weight), a midline spinal puncture was performed at L4/L5 with the patient in the lateral decubitus position using a 26-gauge Quincke spinal needle. We assessed the sensory block with a pinprick, the motor block using the modified Bromage scale, analgesia with the visual analog scale and sedation with the modified Ramsay scale. We also recorded the hemodynamic parameters.

**Results:** The both groups were demographically similar. The time to two segment S2 regression, and rescue analgesia were significant prolonged in group II as compared to group I ( $p < 0.001$ ). Modified Bromage score was significantly higher in group II ( $3.92 \pm 0.15$ ) as compared to group I ( $2.32 \pm 0.19$ ). Patients of both groups were hemodynamically stable throughout the surgery.

**Conclusion:** The intrathecal clonidine in combination with ropivacaine prolongs the duration and quality of spinal anesthesia; it also provides longer duration of postoperative analgesia, without side effects.

**Keyword:** Intrathecal, clonidine, ropivacaine, anorectal surgery

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-4994.2015.00018.9

## INTRODUCTION

Spinal anesthesia has become the preferred anaesthesia for anorectal surgery. Spinal anaesthesia is easy, economical, produces early onset of anesthesia and complete muscle relaxation. Ropivacaine is a new amino amide local anaesthetic. This drug was presented as producing equivalent spinal anesthesia with a faster recovery period than that of bupivacaine. The Intrathecal  $\alpha_2$  agonist clonidine significantly prolongs the duration of both sensory and motor analgesia with ropivacaine. Intrathecally administered local anesthetics has prolongs the duration and antinociceptive properties.<sup>[1],[2],[3]</sup> The intrathecal clonidine is more effective with ropivacaine in comparison to oral and IV route.<sup>[2],[4]</sup> The intrathecal clonidine 1–2 µg/kg adequate dose for Significantly

improve the intensity and increase the duration of sensory and motor blocked provide by local anesthetics.<sup>[1]</sup> However, it is associated with bradycardia, relative hypotension, and sedation. The low-dose intrathecal clonidine in obstetric analgesia, which showed effectiveness without systemic side effects.<sup>[2],[5]</sup> Our study to investigate the minimal effective dose of clonidine to be added to low-dose intrathecal ropivacaine. We hypothesized that intrathecal clonidine 30 µg prolongs spinal anesthesia and analgesia. The primary outcomes of studied were onset and regression of sensory and motor blockade. Secondary outcome were hemodynamic and prolongation of analgesia.

## MATERIAL AND METHODS

Prospective, double-blind, randomized study was performed after getting approval from Ethical Committee and informed consent was taken from all the patients. This study was performed in 120 patients of either sex, aged 18-60 years with belonged to American Society of Anaesthesiology (ASA) grade I to III. None of the patients had any contraindication for spinal anaesthesia. Patients scheduled for elective anorectal surgery were enrolled in the study. Patients were randomized into two groups (n=60 in each group) using computer generated random number

table. In the group I: 0.75% ropivacaine (1ml) with isotonic saline and group II 0.75% ropivacaine (1ml) with 30 µg clonidine. An oral 7.5 mg midazolam premedication was given 2 hours preoperatively. Ringer's lactate hydration solution (15ml/kg body weight), a midline spinal puncture was performed at L4/L5 with the patient in the lateral decubitus position using a 26-gauge Quincke spinal needle. The L4/5 interspace was identified by All patients had spinal anesthesia according to a line between the upper borders of the iliac crest. Duration of anesthesia was measured as the time interval from intrathecal injection to regression of the sensory block below L1. The intensity of pain was assessed using a 10 point VAS. In add sedation was scored on a 5 point scale ranging from 0 to 5 (0 = fully awake, alert to 5 =deeply asleep, not responding to verbal commands).<sup>[6]</sup> Modified Bromage scale was used to assess the motor block (0 = no block, 1 = inability to raise extended leg, 2 = inability to flex knee and 3 = inability to flex ankle and foot).<sup>[7]</sup>

Complications during surgery were treated as follows: hypotension (defined as a systolic blood pressure of <90 mm Hg) was treated with increments of 5mg ephedrine, bradycardia (defined as a heart rate of <50 bpm) was treated with 0.3 mg of atropine, and oxygen desaturation (defined as pulse oximetry oxygen saturation <90% on room air) was treated with oxygen via Hudson's face mask. If a patient complained about discomfort or pain, midazolam 0.05 mg/kg and fentanyl 25µg IV was administered by the anaesthesiologist in incremental doses. Adverse events (hypotension, bradycardia, sedation, nausea and vomiting, shivering and pruritus) were recorded during operation and recovery.

### STATISTICAL ANALYSIS

Statistical analysis was performed by using SPSS software 15. Data are presented as median (range), mean (SD) or frequencies as appropriate. Sensory and motor block characteristics were compared using the Student's *t*-test and non-parametric Mann-Whitney U-test. The demographic data and proportion of side effects was compared

using the chi-square test ( $\chi^2=57.24, 10$ ) and statistical significance was observed at  $P<0.05$ .

### RESULTS

Observations were made from total 120 patients, 60 in each group. The two study groups were comparable with respect to demographic profile. There was no significant difference in age, height, weight, hemodynamic and ASA status in both groups (Table 1).

There was no significant difference in the Time to reach T10 sensory block in groups II ( $5.25 \pm 1.21$ ) compared with group I ( $4.60 \pm 1.04$ ). Onset of motor blockade was not significantly prolonged in group II ( $10.58 \pm 1.87$ ) as compared with group I ( $9.12 \pm 1.75$ ). The time to two segment regression and regression to S2 was significantly prolonged in clonidine groups ( $133.40 \pm 18.84, 263.00 \pm 24.06$ ) as compared to control group ( $104.80 \pm 15.31, 184.40 \pm 22.17$ ) respectively (Table 2). Demand of rescue analgesia was significant prolonged in group II ( $275.75 \pm 25.16$ ) as compared to group II ( $191.65 \pm 18.2$ ). Modified Bromage score was significantly higher in group II ( $3.92 \pm 0.15$ ) as compared to group I ( $2.32 \pm 0.19$ ) while Modified Bromage Score at 2 hours was almost similar in both groups (Table 2).

Patients of both groups were hemodynamically (heart rate and mean arterial blood pressure) stable throughout the surgery (Fig.1, Fig.2). Total requirement of ephedrine in patients were more in group II as compared to group I (Table 3). Supplementation of midazolam, and fentanyl were required in group I for completion of surgery, while patients of group II did not required any analgesic and/or sedative for completion of surgery (Table 3). The surgical anesthesia was graded by anesthetist as superior in group II as compared to group I. Incidence of bradycardia, hypotension and nausea in ropivacaine clonidine combination groups as compared with ropivacaine groups were present but did not significantly difference (Table 4). Vomiting and shivering were not present in both groups (Table 4).

**Table 1: Baseline and Demographic characteristics of two groups**

Characteristics	Group I	Group II	p value
Age (yrs)	49.44 ± 11.52	51.12 ± 10.30	NS
Height (cm)	158.00 ± 21.94	160.64 ± 23.59	NS
Weight (cm)	63.56 ± 8.90	65.64 ± 8.18	NS
Sex Male/Female	41/19	43/17	NS
Heart rate (beats/min)	80.56 ± 1.03	80.88 ± 1.15	NS
Systolic BP (mmHg)	132.12 ± 1.47	132.12 ± 1.79	NS
Diastolic BP (mmHg)	75.60 ± 1.24	76.96 ± 1.22	NS
Mean BP (mmHg)	94.44 ± 1.04	95.01 ± 1.14	NS

ASA physical status: I	20 (40%)	21 (32%)	NS
II	19 (16%)	19 (36%)	
III	21 (44%)	20 (32%)	

NS p&gt;0.05

**Table 2: Characteristic of Spinal Block**

	Group 1	Group 2	p-value
Time to reach T10 sensory blockade (min ± SD)	4.60 ± 1.04	5.25 ± 1.21	p>0.05
Onset of Motor Blockade (min ± SD)	9.12±1.75	10.58±1.87	p>0.05
Time 2 segment regression (min ± SD)	104.80 ± 15.31	133.40 ± 18.84	p<0.001**
Duration of regression to S2 (min ± SD)	184.40 ± 22.17	263.00 ± 24.06	p<0.001**
Rescue Analgesia (min ± SD)	191.65±18.2	275.75±25.16	p<0.001**
Maximum modified Bromage score:	2.32 ± 0.19	3.92 ± 0.15	p<0.05*
Modified Bromage Score at 2 hours	4.14 ± 0.17	4.68 ± 0.10,	P>0.05
Intraoperative VAS Score	1.36 ± 0.20	0.56 ± 0.13	p<0.05*

\*\* P&lt; 0.001, \* p&lt;0.05

**Table 3: Analgesia requirement**

No. of Patients	Group I	Group II
Ephedrine requirement	0 (0%)	3 (1.8%)
Fentanyl requirement	2 (1.2%)	0 (0)
Midazolam requirement	5 (3%)	0 (0)

**Table 4: Adverse effects**

	Group I		Group II	
	No.	%	No.	%
Bradycardia	0	0	1	0.6
Hypotension	0	0	4	2.4
Nausea	0	0	2	1.2
Vomiting	0	0	0	0
Shivering	0	0	0	0
Post Dural puncture headache	0	0	0	0

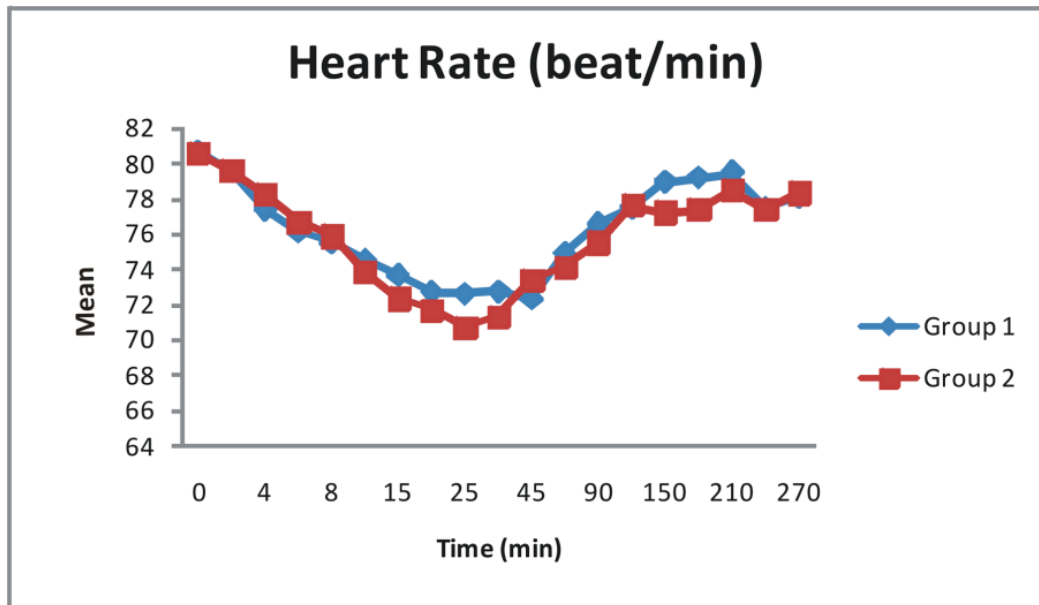


Fig. 1: Heart Rate Summary

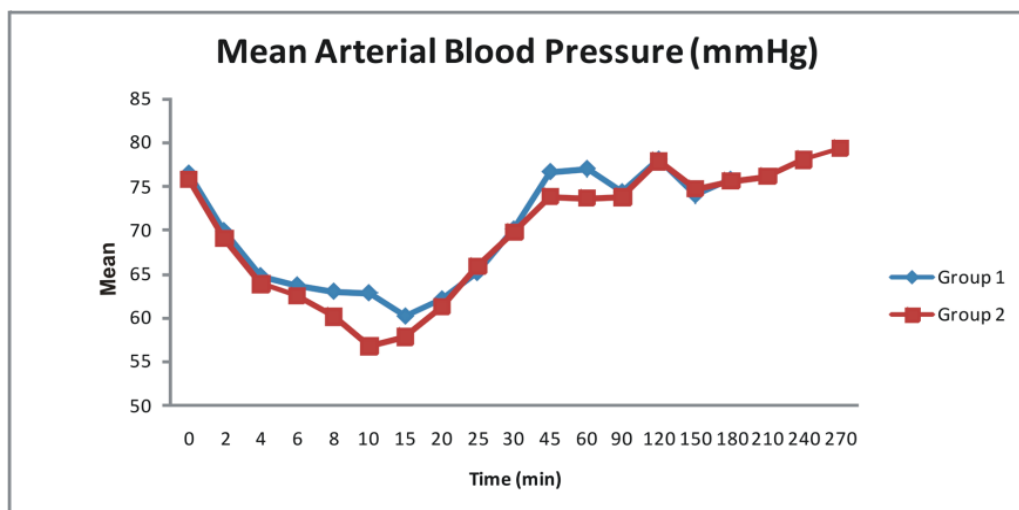


Fig. 2: Mean Arterial Blood Pressure Summary

## DISCUSSION

The intrathecal clonidine ( $\alpha_2$ -adrenergic agonist) along with local anaesthetics increases the quality and the duration of the anaesthesia.<sup>[1],[3],[5]</sup> Clonidine 1 mcg/kg with ropivacaine 0.1% prolongs the duration and quality of analgesia compared to plain ropivacaine 0.1% and 0.2% without any significant sedation.<sup>[8]</sup> Intrathecal clonidine prolongs spinal analgesia (sensory and motor block) with ropivacaine.<sup>[9],[10]</sup> However, they are associated with higher incidence of hypotension and bradycardia. Other potential side effects include nausea, vomiting, sedation and respiratory depression, especially if higher doses are used.

Intrathecal clonidine has been used in conjugation with various local anaesthetics in dose between 15 $\mu$ g to as high as 150 $\mu$ g and has been shown

to prolong the time to 2 segment regression, sensory block regression to L2, duration of analgesia, and reduce the incidence of intraoperative pain.<sup>[11]</sup> The duration of sensory blockade (defined as regression to S1 sensory dermatome) is prolonged by adding dexmedetomidine (303  $\pm$  75 minutes) and clonidine (272  $\pm$  38 minutes) when compared to control (190  $\pm$  48 minutes).<sup>[12]</sup> However the difference between the study groups receiving clonidine and dexmedetomidine was not statistically significant. De Kock et al. studied that various doses of clonidine (15 $\mu$ g, 45 $\mu$ g and 75 $\mu$ g as an additive to 8 mg ropivacaine), increased the two segment sensory regression compared to control group (8 mg ropivacaine). But this increase was not dose dependent.<sup>[10]</sup> Small doses of intrathecal clonidine ( $\leq$ 150 $\mu$ g) significantly prolong the anesthetic and analgesic effects of

bupivacaine in a dose-dependent manner and that 150 µg of clonidine seems to be the preferred dose, in terms of effect versus unwarranted side effects, when prolongation of spinal anesthesia is desired.<sup>[13]</sup> The intrathecal application of clonidine in combination with bupivacaine improves the duration and quality of spinal anesthesia.<sup>[14,15]</sup> The addition of clonidine to 0.1% ropivacaine gives similar quality and duration of analgesia as that of 0.2% ropivacaine and clonidine, without causing significant degree of post-operative sedation and motor weakness.<sup>[16,17]</sup> The duration of motor block was prolonged with clonidine (10 min) group than in the control group (153 +/- 26 min vs. 131 +/- 29 min, P < 0.05).

In our study we observed the time to two segment regression and regression to S2 was significantly prolonged in groups II as compared to group I. Demand of rescue analgesia was also significant prolonged in group I as compared to group II. Onset of sensory block and motor blockade was almost similar effect in both groups.

The lowest heart rate and mean blood pressure were not different among groups.<sup>[18]</sup> Bradycardia, hypotension, and sedation were not recorded in both groups I (clonidine 2µg/kg with 1% ropivacaine 1ml/kg) compared with group II (clonidine 2µg/kg with 0.2% ropivacaine 1ml/kg).<sup>[16]</sup> There was hemodynamic stable in all groups (group A received 1 ml/kg of 0.1% ropivacaine, group B received 1 ml/kg of 0.1% ropivacaine with clonidine 1 mcg/kg, and group C received 1 ml/kg of 0.2% ropivacaine).<sup>[8]</sup> Kanazi et al. concluded in their study that addition of 3µg dexmedetomidine or 15µg clonidine to 12 mg bupivacaine did not produce significant change in heart rate.<sup>[18]</sup> The risk of bradycardia was not significantly increased in patients who received intrathecal clonidine.<sup>[11]</sup> The hemodynamic stability was similar in both groups bupivacaine 0.5% (7.5 mg) and bupivacaine (7.5 mg) with clonidine (25 µg).<sup>[14]</sup> In our study, we also found the similar effects, both groups are hemodynamic stable. Bradycardia, hypotension, sedation, nausea and vomiting were not recorded in both groups.

## CONCLUSION

The addition of low dose intrathecal clonidine (30 µg) in combination with ropivacaine (0.75%) for anorectal surgery significantly prolongs the duration and quality of spinal anesthesia; it also provides longer duration of two segment regression, rescue analgesia and postoperative analgesia, early mobilisation without significant side effects. We conclude that small doses of clonidine with ropivacaine can be used safely for anorectal surgery.

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