Original Research Article

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Effect of intrathecal Clonidine on subarachnoid Block Characteristics in Patients Undergoing TURP and TURBT

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Abstract

Introduction: Transurethral resection of prostrate (Turp) and transurethral resection bladder tumour (Turbt) are major operations, subarachnoid block is a well accepted and popular technique for Turp and Turbt. *Materials and method:* This randomized prospective double blind study conducted at MIOT hospitals, Chennai, from October 2014 – December 2015, evaluated the effective dose of clonidine with 10mg of 0.5% heavy bupivacaine in 80 patients posted for these surgeries and also to find the effect of various doses of clonidine on various subarachnoid block characteristics. *Results:* The level of peak sensory block (mean ± SD) was thoracic vertebral level T9.4 ± 0.68 in group BN T8.95 ± 0.94 In group BC 15, T8.3 ± 1.41 in group BC 25 and T7.5 ± 1.19 in group BC 35. There were significant differences in the peak sensory level between the groups. The 2 segment regression time (mean ± SD) defined as the time taken for the peak sensory level to regress 2 segments was compared between the 4 groups. It was 53.65 ± 5.81 min in group BN compared to 56.15 ± 7.23 min in groupBC15, 63.60 ± 8.66 min in group BC 25 and min 65.25 ± 6.87 in group BC 35. The difference in 2 segment regression was significant between the groups. The time to first requirement of analgesia was compared the 4 groups. It was 85.95 ± 6.21 min in group BN, 89.25 ± 6.37 min in group BC 15, 95.90 ± 8.59 min in group BC 25, 99.50 ± 5.72 min in group BC 35 . The difference was significant between the groups. *Conclusion:* Addition of 35mcg of clonidine to bupivacaine when compared to 25mcg/15mcg clonidine significantly prolongs the duration of analgesia without affecting the onset and maximum level achieved of sensory block.

Keywords: Intrathecal clonidine; TURP; TURBT

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Introduction

Transurethral resection of prostrate (Turp) and transurethral resection bladder tumour (Turbt) are major operations, subarachnoid block is a well accepted and popular technique for Turp and TURBT, that can be performed under general anaesthesia and epidural anaesthesia also.[1,2]

Intrathecal bupivacaine is commonly used for subarachnoid block, however doses more than 10 mg are associatedwith prolonged sensory and motor blockade so we are restricting bupivacainedose in this study to 10mg.[3] Various agents such as Opioids, Clonidine, Ketamine, Midazolam, Neostigmine were used as adjuvants to Bupivacaine in subarachnoid block.

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Clonidine is an alpha 2(α-2) adrenoreceptor agonist. Alpha 2 adrenoreceptors are located on primary afferent terminals on neurons in the superficial lamina of the spinal cord and within several brainstem nuclei. They may be responsible for analgesicaction at peripheral spinal and brainstem sites[4]. Clonidine produces a minor degree of nerve conduction blockade at high concentrations with some preference to C fibers.[4] This conduction blockade may result in the enhancement of peripheral nerve block when this agent is added to local anaesthetics.[5] Clonidine not only prolongs the duration of action of bupivacaine but also has potent antinociceptive properties.

Materials and methods

This randomized prospective double blind study conducted at MIOT hospitals, Chennai, from October 2014 – December 2015, evaluated the effective dose of clonidine with 10mg of 0.5% heavy bupivacaine in 80 patients posted for these surgeries and also to find the effect of various doses of clonidine on various subarachnoid block characteristics. Patients of either physical status ASA 1 or ASA 2 admitted for elective Turp and Turbt.

Formula used for the sample size n:

$n = (Z_{\alpha/2} \pm Z_{\beta})^2 * 2 * \sigma^2 / d^2$

where $Z_{\alpha/2}$ is the critical value of the Normal distribution at α/2 (e.g. for a confidence level of 95%, α is 0.05 and the critical value is 1.96), Z_{β} is the critical value of the Normal distribution at β (e.g. for a power of 80%, β is 0.2 and the critical value is 0.84), σ_2 is the population variance, and d is the difference you would like to detect

Patients of ASA physical status 1 and 2, were included in the study. while the patients of ASA physical status 3 and above, allergic to any of the study drugs, undergoing treatment with α2 agonists, patients refusing for the trial, coming with emergency bladder outlet obstruction, Patients with Absolute contraindication for spinal anesthesia-Raised ICT, Bleeding disorders, and Infection at the site, Neurological deficit were excluded from the study.

After institutional ethics committee approval and informed consent 80 patients were included in the study. Patients were randomized to one of the four groups according to a computer generated randomization list

- Group BN: 10mg (2ml) 0.5% hyperbaric bupivacaine ± normal saline(0.24ml)
- Group BC15: 10mg (2ml) 0.5% hyperbaric bupivacaine ± 15μg clonidine (diluted with normal saline to 0.24ml).
- Group BC25: 10mg (2ml) 0.5% hyperbaric bupivacaine ± 25μg clonidine (diluted with normal saline to 0.24ml).
- Group BC35 : 10mg(2ml) 0.5% hyperbaric bupivacaine ± 35μg clonidine

Each patient was advised to fast after 10pm and diazepam [5-10mg] given orally night before surgery and 2 hrs before surgery. All patients [ie; patients in group BN, BC15, BC25, BC35] received 2ml bupivacaine ± additive(normal saline/ clonidine) intrathecally over 1 minute after ensuring free flow of cerebro spinal fluid (CSF) .The patient was then positioned supine and the level of sensory and motor blockade were assessed. The cephalad spread of anaesthesia and the degree of motor block was assessed every 5 min. The level of sensory block was assessed by pin prick using 25 G needle. The onset of motor blockade noted as the time taken for loss of knee reflex. [Modified bromage score 3]. The maximum height of the blockade was determined by the sensory level achieved at 20 min. All patients were monitored in PACU after the Surgery for a period of 24hrs. postoperative pain, Duration of pain relief, Any symptom of TURP SYNDROME, Time for catheter sensation and Adverse effects were noted finally.

Results

The mean age of patients(± SD) in group BN was 44.95 ± 15.34 years compared to 47.15 ± 15.15 years in group BC15, 45.10 ±14.46 years in groupBC25 and 43.20 ± 16.67 years in group BC35. The difference in age between the groups was not significant. The gender distribution was comparable between the groups.

The distribution of patients according to ASA physical status between the groups was also comparable. 7 patients in group BN,7 patients in group BC15 , 11 patients in group BC25 and 8 patients in group BC35 belonged to ASA physical status 2 and mainly had controlled essential hypertension.

The mean weight in kilograms of patients in group BN was 77.50 ± 15as compared to 72.50 ± 8 in group BC15, 75.85 ± 11.47 in group BC25 and 72.05 ± 9.19 in groupBC35. The difference in weight between the groups was not significant.

The Duration of Surgery Between the 4 Groups was of mean Duration of 42.60 ± 5.67 min in Group BN, 46 ± 6.58mins in group BC15, 46.85 ± 7 ins in group BC25 and 52 ± 7.17 mins in Group BC35 (Table 1 and Fig. 1).

Table 1. Demographic data

Parameters	Group BN	Group BC15	Group BC25	Group BC35	*p* Value
Age	44.95 ± 15.34	47.15 ± 15.15	45.10 ± 14.46	43.20 ± 16.67	NS
Gender (M/F)	2/10	2/10	2/10	2/10	NS
ASA (1/2)	13/7	13/7	9/11	12/8	NS
Weight	77.50 ± 15	72.50 ± 8	75.85 ± 11.47	72.05 ± 9.19	NS
Surgical duration (min)	42.60 ± 5.67	46 ± 6.58	46.85 ± 7	52 ± 7.17	0.000

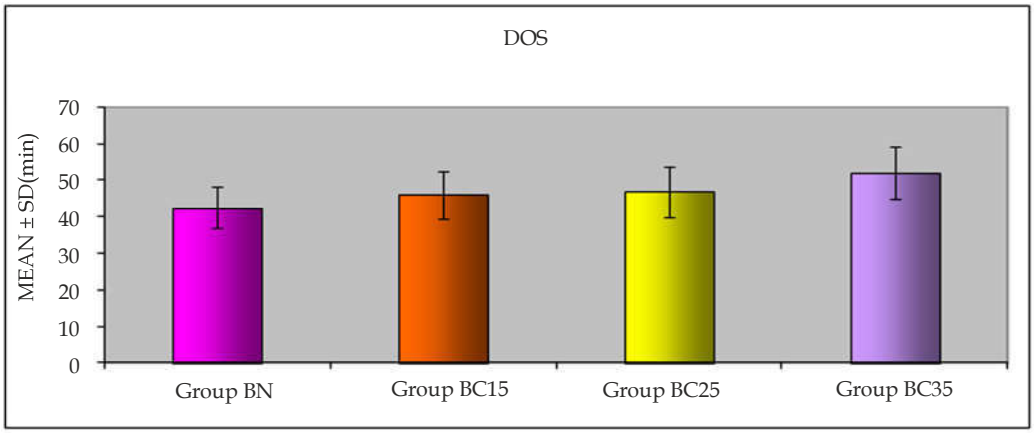

Fig.1: Demographic data

Table 2. Sensory Level

SL	Group BN	Group BC15	Group BC25	Group 35	P
5	11.3 ± 0.5	11.2 ± 0.6	10.1 ± 0.7	9.7 ± 0.5	0.000
10	10.8 ± 0.6	10.4 ± 0.6	9.6 ± 0.8	9 ± 0.6	0.000
15	10.1 ± 0.6	9.7 ± 0.7	8.7 ± 1	8.1 ± 0.8	0.003
20	9.4 ± 0.6	8.9 ± 0.9	8.3 ± 1.4	7.5 ± 1.1	0.000
25	8.8 ± 0.5	8.2 ± 0.6	7.4 ± 1	6.8 ± 1.1	0.001
30	8.4 ± 0.6	7.8 ± 0.7	7 ± 1.3	6.4 ± 1	0.000
35	7.8 ± 0.6	7.5 ± 0.6	6.2 ± 1.3	5.8 ± 0.7	0.000
40	7.7 ± 0.6	8 ± 0.9	6 ± 1.1	5.4 ± 0.8	0.000
45	8.1 ± 0.5	8.5 ± 0.8	6.4 ± 0.9	5.6 ± 1	0.000
50	8.3 ± 0.5	9.3 ± 0.8	7 ± 0.7	6.1 ± 0.8	0.000
55	9 ± 1.4	9.7 ± 0.9	6.8 ± 0.4	6.5 ± 0.7	0.032
60			7.8 ± 0.4	7.1 ± 0.6	0.146

p value <0.05 significant SL = sensory level.

Sensory block characteristics: The level of peak sensory block(mean ± SD) was thoracic vertebral level T9.4 ± 0.68 in group BN T8.95 ± 0.94 In group BC15, T8.3 ± 1.41 in groupBC25 and T7.5 ± 1.19 in group BC35. There were significant differences in the peak sensory level between the groups. The minimum level of sensory block achieved at 20 minutes was T10 in all 4 groups. The maximum level of sensory block achieved was T8 in group BN T6 in group BC15, T4 in group BC25 and Group BC35 at 20 minutes. The sensory level was checked with pin prick method every 5 min thereafter. The sensory block level achieved in all 4 groups was comparable up to 50-60 minutes. Sub group analysis showed significant differences in sensory block level between the groups BN and BC35 from 05 minutes onwards. There were no significant differences between groups BNand BC15, B15 and BC25, B25 and BC35. The mean sensory level (mean ± SD) is shown in table 2 and displayed graphically in Figure 2.

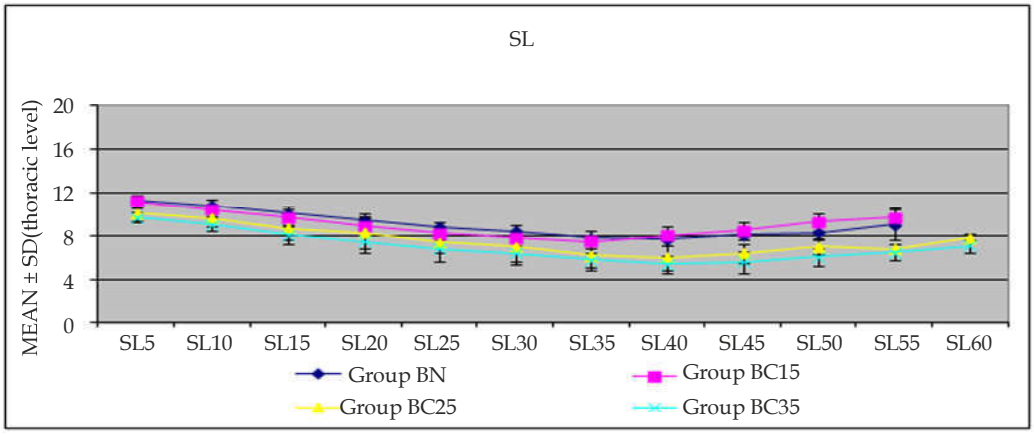

Fig. 2: Sensory Level

Table 3: Two Segment Regression Time

Parameter	MEAN ± SD				*p* Value
	BN	BC15	BC25	BC35	
Duration (Mins)	53.65 + 5.81	56.15 + 7.23	63.60 + 8.66	65.25+6.87	0.000

p Value <0.05 is significant.

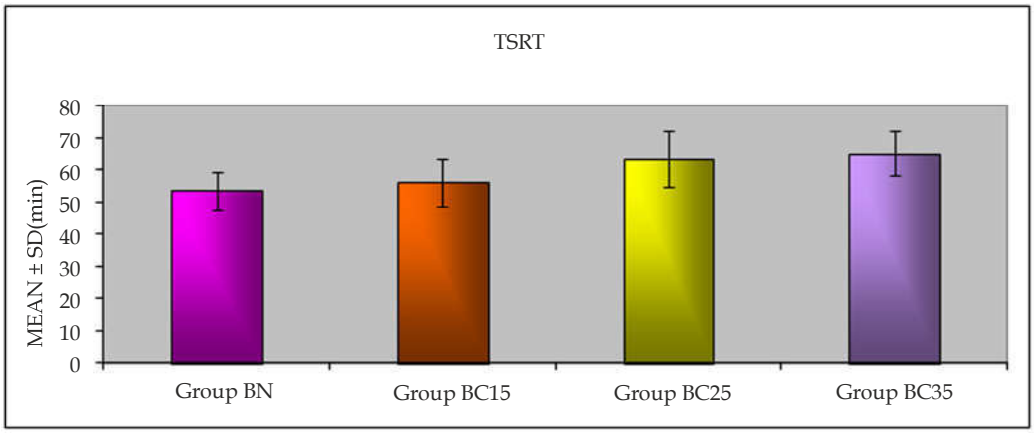

Fig. 3: Two Segment Regression Time

Two segment regression time: The 2 segment regression time (mean ± SD) defined as the time taken for the peak sensory level to regress 2 segments was compared between the 4 groups. It was 53.65 ± 5.81 min in group BN compared to 56.15 ± 7.23 min in Group BC15, 63.60 ± 8.66 min in Group BC25 and min 65.25 ± 6.87 in group BC35. The difference in 2 segment regression was significant between the groups. Subgroup analysis showed a significant difference in 2 segment regression times between groups BN and BC25 and BN and BC35. It was not statistically significant between groups BN, BC15 and BC25, BC35. The 2 segment regression time (mean ± SD) is tabulated in Table 3, and displayed in Fig. 3.

Time to first requirement of analgesia: The time to First requirement of analgesia was compared the 4 groups. It was 85.95 ± 6.21 min in group BN, 89.25 ± 6.37 min in group BC15, 95.90 ± 8.59 min in group BC25, 99.50 ± 5.72 min in group BC35. The difference Was significant between the groups. Subgroup analysis was done and there was a significant difference in the time to first requirement of analgesia between the Groups BN & BC25 and BN & BC35. It was not significant between the groups BN & BC15 and BC15 & BC25. The time to first requirement of analgesia (Mean ± SD) is tabulated in Table 4, and is displayed graphically in Figure 4.

Table 4: Time to first requirement of analgesia

Parameter	MEAN ± SD				*p* Value
	BN	BC15	BC25	BC35	
Duration(Mins)	85.95+6.21	89.25+6.37	95.90+8.59	99.50+5.72	0.000

p Value <0.05 Significant

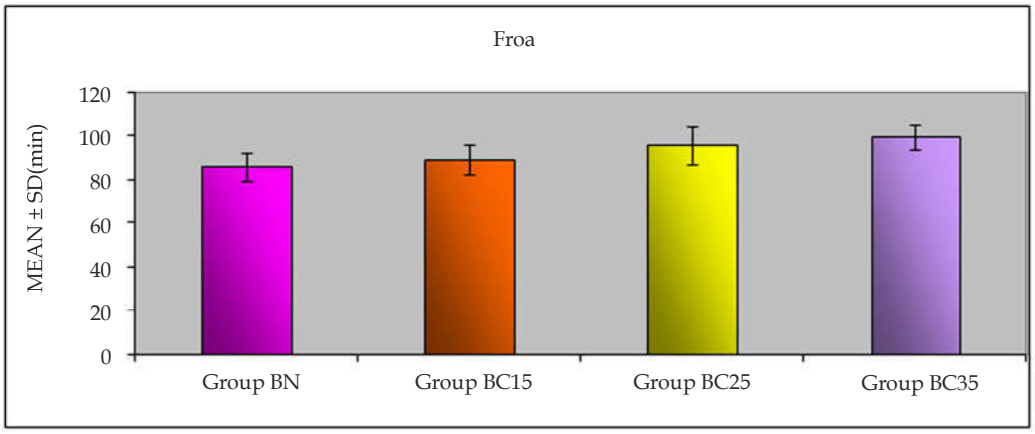

Fig. 4: Time to first requirement of analgesia

Table 5: Duration of Motor Block

Parameter	**MEAN ± SD**				***p* Value**
	BN	**BC15**	**BC25**	**BC35**	
Duration(Mins)	89.90 + 6.19	98.5 + 7.09	120 + 10.40	133.75 + 17.32	0.000

p Value <0.05 Significant

Significant difference was observed with BC35 from others. NO significant difference is seen between BN and BC15 groups.

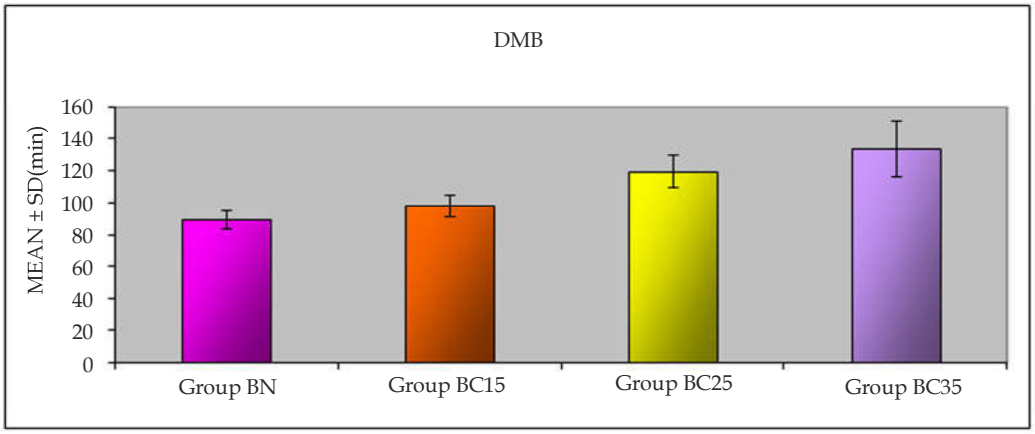

Fig. 5: Duration of Motor Block

Motor block charecteristics: In group BN it was 89.90 ± 6.19 mins, 98.5 ± 7.09 mins in group BC15, 120 ± 10.40 mins in group BC25 and 133.75 ±17.32mins in groupBC35. The motor block characteristics (mean ± SD) is tabulated in table 5, and displayed graphically in Figure 5.

Discussion

The addition of clonidine to intrathecal bupivacaine prolongs the duration of motor block by 30-50%[6]. The mechanism is due to the alpha 2 adrenoreceptor induced hyperpolarisation of motor neurons in the ventral horn of spinal cord.[7] However these studies have used higher doses of local anesthetics (15mg) along with higher doses of clonidine (75mcg) for patients undergoing lower limb and lower abdominal surgeries[6].

There are a limited number of studies in literature

in which lower doses of intrathecal clonidine has been used as an adjuvant with hyperbaric bupivacaine for transurethral resection of prostrate (TURP) and transurethral resection of bladder tumor (TURBT). Our study compared the effects of addition of various doses of clonidine 15mcg, 25mcg and 35mcg to hyperbaric bupivacaine 0.5% 10mg on subarachnoid block characteristics in patients undergoing TURP and TURBT. Eighty patients were randomly selected and assigned into four groups (BN, BC15, BC25 and BC35). We found that patients in group BC35 had a longer two segment regression time, longer duration of motorblockade and longer time for first analgesic requirement when compared to other groups.

Sensory blockade is produced by local anesthetics is potentiated by clonidine intrathecally. Mechanism is not known but it is presumed to involve inhibition of afferent neurons at the dorsal horn level resulting in the activation of descending noradrenergic pathways with release of acetylcholine producing analgesia.[8]

In this study the sensory block achieved at 20 mins in all the four groups was comparable. The level of peak sensory block (mean ± SD) was thoracic vertebral level T9.4 ± 0.68 in group NS T8.95 ± 0.94 In group BC15, T8.3 ± 1.41 in groupBC25 and T7.5 ± 1.19 in group BC35.

The minimum level of sensory block achieved at 20 min was T10 in all 4 groups. The maximum level of block achieved was T8 in group NS, T6 in group BC15, T4 in group BC25 and group BC35 at 20 mins. The sensory block level achieved in all 4 groups was comparable upto 55mins. There was a significant difference in sensory level between the groups NS and BC35 starting from 05 min onwards.

The effect of intrathecal clonidine in increasing the duration of sensory blockade is more marked with doses > 75 mcg. Lower doses have shown heterogeneous results in terms of prolongation of sensory block.[9]

Braz and coworkers[9] found that addition of 45 mcg or 75 mcg of clonidine to 17.5 mg of hyperbaric bupivacaine resulted in almost similar increase in the two segment regression times as compared to bupivacaine alone in patients undergoing cesarean section.

Ajay kumarchowdary and coworkers[10] did a study in patients under going elective anorectal surgery and found that the time to two segment S2 regression, was significant prolonged in patients receiving 30 mcg of intrathecal clonidine with 0.75% ropivacaine than in patients receiving 0.75% ropivacaine alone.

The time to first requirement of analgesia was compared the 4 groups. It was85.95 ± 6.21 min in group BN, 89.25 ± 6.37 min in group BC15, 95.90 ± 8.59 min in group BC25, 99.50 ± 5.72 min in group BC35 . The difference was significant between the groups.

Subgroup analysis was done and there was a significant difference in the time to first requirement of analgesia between the groups BN & BC25 and BN & BC35. It was not significant between the groups BN & BC15 and BC15 & BC25.

Manishasapate and coworkers[11] did a study and found that the time to first requirement of analgesiawas considerably prolonged in Group receiving clonidine (450.33 ± 95.10 min) as compared with Group receiving plain hyperbaric bupivacaine (220 ± 36.36 min), which was also highly significant. The total duration of analgesia was prolonged in this study in all the three groups who were given clonidine.

Conclusion

Addition of 35mcg of clonidine to bupivacaine when compared to 25mcg/15mcg clonidine significantly prolongs the duration of analgesia without affecting the onset and maximum level achieved of sensory block. Postoperative analgesia was also prolonged with 35mcg clonidine with an increase in motor block duration (as evidenced by longer time for first analgesic requirement) in patients undergoing transurethral resection of prostrate (TURP) and transurethral resection of bladder tumour (TURBT).

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