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Effects of Clonidine on Spinal Anesthesia with Hyperbaric Bupivacaine

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Abstract

Background: Clonidine is one of the drugs that have been extensively studied by administering through oral, intravenous and intrathecal routes to prolong the spinal anesthesia. A lot of studies have shown oral clonidine premedication to prolong duration of sensory block and motor block. This study is undertaken to evaluate the effect of oral clonidine as premedicant on spinal anesthesia with 0.5% hyperbaric bupivacaine. *Methods:* A double blind randomized controlled study was carried out on 100 participants who underwent elective surgeries under spinal anesthesia. The participants were allocated into experimental (oral Clonidine) and control group (50 each) equally. Heart rate, level and duration of sensory and motor blockades were observed. *Results:* The mean time to highest sensory blockade was lower in experimental group (5.28 min) when compared to control group (7.76 min). The observed difference was statistically significant (p<0.001). Similarly, there was a statistically significant difference in the mean duration of motor blockade between the groups, wherein the experimental group had a longer duration (264 min) compared to the control group (208.50 min) (Table 4). *Conclusion:* Premedication with oral clonidine 150µg, 1 hour prior to spinal anesthesia is adequate to provide clinically useful prolongation of sensory blockade without significant adverse effects.

Keywords: Clonidine; Pre-medication; Sensory blockade; Spinal anesthesia.

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Introduction

Spinal anesthesia during initial days was mainly performed using local anaesthetics. Later interest developed with regard to adding additives to local anaesthetics, to prolong spinal anesthesia. In the context of "Augmentation strategies" for epidural and intrathecal analgesia, discovery of opioid receptors and the subsequent development of epidural and intrathecal opioid administration is undoubtedly one of the most significant advances in pain management in the last three decades.[1]

The alpha 2 agonist clonidine has shown properties that are potentially beneficial for oral premedication to reduce sympathetic activity, shivering, and oxygen consumption during recovery from anesthesia. In addition, Clonidine does not result in drying of secretions; minimizes fluctuations in the haemodynamic profile during anaesthetic induction and decreases the anaesthetic

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requirements of both opioid and volatile anaesthetics. Clonidine provides significant benefits for preoperative anxiety and analgesia.[2]

Clonidine is one of the drugs that have been extensively studied by administering through oral, intravenous and intrathecal routes to prolong the duration of action of spinal anesthesia. However, it is of interest to find the effectiveness of oral clonidine given as a premedicant on the duration of bupivacaine spinal anesthesia. A lot of studies have shown oral clonidine premedication to prolong duration of sensory block and motor block.[3-5] This study was undertaken to evaluate the effect of oral clonidine as a premedicant, on spinal anesthesia with 0.5% hyperbaric bupivacaine.

Objectives

This study was carried out to assess following effects of oral clonidine (150 µg), as a premedicant on hyperbaric bupivacaine (0.5%) spinal anesthesia.

1. Onset and duration of sensory and motor blockade.
2. Haemodynamic effects.

Materials and Methods

Study design and participants

A double blind randomized controlled study was carried out in the Department of Anaesthesiology of a tertiary teaching institution for a period of one year. All the patients who underwent elective surgeries under spinal anesthesia during the study period were selected for the study. A total of 100 patients participated in the study.

Inclusion criteria

1. Age between 20-60 years
2. ASA I & II patients
3. Elective lower abdominal and lower limb surgeries performed in supine position
4. Weight: 40 – 60 kg
5. Height: Around 150 cm

Exclusion criteria

1. ASA III & IV patients
2. Hypertensive patients on beta blockers, calcium channel blockers
3. Patients on digoxin
4. Patients who require opioids, intravenous or inhalational anaesthetics as supplementation for regional anesthesia
5. Patients who had inadequate block requiring general anesthesia.

Randomization and sampling

The participants were allocated into experimental and control group equally. Randomization was carried out based on computer generated random numbers. Each group consisted of 50 participants.

Group A (Control): Placebo and 3 ml (15 mg) hyperbaric bupivacaine (0.5%) spinal anesthesia.

Group B (Experiment): Oral clonidine (150 µg) as premedicant and 3 ml (15 mg) hyperbaric bupivacaine (0.5%) spinal anesthesia.

Ethical approval and informed consent

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

Procedure

The participants were pre-medicated the previous night with T. Alprazolam 0.5 mg HS and Inj. Ranitidine 50 mg intravenous and Inj. Ondansetron 4 mg was administered intravenously 30 minutes before shifting to operation theatre. Baseline parameters, namely heart rate, non invasive blood pressure (NIBP) and SpO_2 were recorded before pre-medication. Oral Clonidine (150 µg) with sips of water was administered to the participants in the experimental group, 60 minutes before anesthesia. Preloading was done with 10 – 15 ml/kg of Ringer's Lactate solution over thirty minutes followed by infusion of 8 – 10 ml/kg/hour intravenously as maintenance fluid. HR and BP recorded just before spinal anesthesia was taken as "0" min reading. Under aseptic precautions, lumbar puncture was done in the lateral position at L2-L3 space, using 26 G Quincke's spinal needle. 3 ml of 0.5% hyperbaric bupivacaine was injected at the rate of 1ml in 3 sec with table flat and patient was immediately turned supine and supplemental oxygen started.

Data collection

Haemodynamic monitoring: Continuous monitoring of ECG, HR, SpO_2, NIBP was carried out. *Hypotension* was defined as decrease in SBP of > 30% from the baseline value and was treated with bolus intravenous fluid and intravenous bolus dose of

Inj. Ephedrine 6 mg. *Bradycardia* was defined as HR <60/min; recorded and treated with intravenous Inj. Atropine 0.6 mg.

Sensory blockade (*elicited by pin prick*): Dermatome levels of sensory anesthesia were checked every five minutes for the first thirty minutes, every 10 minutes during the intraoperative period and every fifteen minutes thereafter till the level regresses to L1 dermatome. Highest level of sensory block was noted. Onset of sensory blockade was considered as the time in minutes from injection of the intrathecal drug to the time for the block to attain its highest level. Duration of sensory blockade was time interval between the onset of sensory blockade to regression to L1.

Motor blockade (*assessed by Bromage score*): Motor blockade was assessed every five minutes for the first thirty minutes, and every 10 minutes during the intra operative period and every fifteen minutes thereafter till complete recovery from motor blockade.[4] Onset of motor blockade was noted as the time taken from the deposition of intrathecal drug to time taken to reach grade 3 motor blockade. Duration of motor blockade was noted as the time interval between onset of grade 3 motor blockade to complete recovery from motor blockade. The Bromage scoring is given in table 1.

Table 1: Bromage score for the study participants:

S. No	Score	Interpretation
1	0	No change in movement of legs and feet
2	1	Barely able to flex knees. No foot movement change
3	2	Unable to flex knees and barely move feet
4	3	Unable to move feet and knees

Data analysis

Data was entered and analyzed using SPSS version 20 software. Results on continuous data were presented as mean values. Independent sample t test and chi square test were used to evaluate the statistical significance between the groups. A p value < 0.05 was considered statistically significant.

Results

Majority of the participants in both the groups were males and belonged to ASA I. (Table 2). Both the groups were comparable with respect to their background characteristics. The mean age of the participants in group A was 37.2 years while the same in group B was 38.3 years. The mean body weight and mean height were also similar between the groups (Table 3).

Majority of the participants underwent herniorraphy (56% and 52% in Groups A & B respectively). In majority of participants the sensory level of blockade was achieved at the level of T6 (72% and 68% in Groups A & B respectively) (Table 4).

The mean time to highest sensory blockade was lower in experimental group (5.28 min) compared to control group (7.76 min). The observed difference was statistically significant (p<0.001). There was a statistically significant difference in the mean duration of sensory blockade between the groups, wherein the experimental group had a longer duration (223 min) compared to the control group (141.30 min). Similarly, there was a statistically significant difference in the mean duration of motor blockade, wherein the experimental group had a longer duration (264 min) compared to the control group (208.50 min) (Table 5).

Our study showed a significant difference in the mean heart rates between the groups throughout the duration of anesthesia. It was observed that the mean heart rates were lower in the experimental group compared to the control group throughout the anesthetic period (p < 0.05) (Table 6).

Table 2: Background characteristics of the study participants

S. No	Characteristics	Group A N (50)	Group B N (50)	p value
1	*Gender*			
	Male	32(64.0)	34(68.0)	0.673
	Female	18(36.0)	16(32.0)	
2	*ASA distribution*			
	ASA I	38(76.0)	36(72.0)	0.648
	ASA II	12(24.0)	14(28.0)	

Table 3: Mean value of Background characteristics of the study participants

S. No	Characteristics	Group A N (50)	Group B N (50)	*p* value
1	Mean age (years)	37.20 ± 10.65	38.33 ± 9.67	0.583
2	Mean weigh (kg)	68.42 ± 10.25	68.14 ± 10.80	0.894
3	Mean height (cm)	159.48 ± 7.49	158.62 ± 5.99	0.528

Table 4: Distribution of surgical procedures and anaesthetic characteristics of two groups

S. No	Characteristics	No of patients in Group A N(50)	No of patients in Group B N(50)
1	*Type of surgery*		
	Appendicectomy	11(22.0)	12(24.0)
	Herniorraphy	28(56.0)	26(52.0)
	Varicose veins (ligation & stripping)	6(12.0)	5(10.0)
	Fracture tibia(ORIF)	5(10.0)	7(14.0)
2	*Highest sensory level*		
	T4	3(6.0)	5(10.0)
	T5	6(12.0)	5(10.0)
	T6	36(72.0)	34(68.0)
	T7	3(6.0)	2(4.0)
	T8	2(4.0)	4(8.0)
3	*Complications*		
	Bradycardia (HR < 60/min)	6(12.0)	6(12.0)
	Hypotension (Fall in SBP > 30% of baseline)	2(4.0)	3(6)
	Nausea	4(8.0)	5(10.0)
	Vomiting	0	0
	Shivering	4(8.0)	3(6.0)
	No complications	34(68.0)	33(66.0)
4	*Drugs*		
	Atropine (0.6 mg)	6(12.0)	6(12.0)
	Ephedrine (6 mg)	2(4.0)	3(6.0)
	No drugs	42(84.0)	41(82.0)

Table 5: Comparison of duration of motor and sensory blockade between the groups:

S. No	Parameters	Group A	Group B	*p* value	T test
1	Time to highest sensory level (min)	7.76 ± 1.31	5.28 ± 1.89	0.001	8.258
2	Time to regression to L1 (min)	141.00 ± 10.93	223.30 ± 15.24	0.001	31.033
3	Time to grade 3 motor block (min)	5.60 ± 1.21	5.40 ± 1.29	0.727	0.797
4	Duration of motor blockade (min)	208.50 ± 8.16	264.00 ± 11.34	0.001	28.092

Table 6: Mean heart rate (HR) in the two groups at various time intervals

S. No	Time intervals	Group A N(50)		Group B N(50)		*p* value
		Mean HR	SD	Mean HR	SD	
1	0 minute	90.82	9.14	87.34	7.82	0.044
2	60 minute	89.36	8.63	83.70	7.4	0.001
3	90 minute	89.90	8.72	84.00	8.46	0.001
4	120 minute	90.12	8.78	82.82	8.48	0.001
5	180 minute	90.01	8.71	84.20	8.47	0.001

Discussion

The α-2 agonist Clonidine has shown properties that have potential applications as an oral premedication. A lot of studies have shown that premedication with Oral Clonidine prolongs the duration of sensory and motor blockade. In our study, oral clonidine dose of 150 µg was administered to the experimental group patients. The mean time taken to achieve the highest level of sensory blockade was lower in the Clonidine group when compared to the controls ($p<0.001$). However, for the existing dosage, our study could not demonstrate significant changes in the hemodynamic parameters between the Clonidine and control groups.

Manish[3] in his study found the time to highest sensory level in the placebo group was 7.3 ± 0.9 min and in patients pre medicated with clonidine it was 4.2 ± 0.5 min. This study showed that the clonidine group of patients had significantly faster onset of sensory blockade[4]. Harbhej[4] found that time to highest sensory level was lower in the Clonidine group, similar to our study. Similar results were obtained in studies done by Koichi Ota[5] and Singh H[6].

Our study demonstrated a very strong statistically significant difference between the two groups as suggested by the ***p***-value of <0.001 indicating that duration of sensory blockade was significantly prolonged in the clonidie group of patients[3,4,7,8].

Our study compared the total duration of motor blockade between the two groups of patients. Patients in control group had motor block for duration of 208 ± 8.16 min as compared to patients in clonidine group who had motor block for a longer duration of 264 ± 11.34 min. On statistical analysis there was a very strong statistically significant difference between the two groups as suggested by the *p*-value of < 0.001[3,4,6,8].

In our study, the heart rate of patients in the two groups at various time intervals was compared. The mean heart rate in the clonidine group of patients was significantly less at time interval of 0, 60, 90, 120 and 180 minutes compared to the control group patients. The significant decrease in heart rate in the patients premedicated with clonidine could be due to the centrally mediated effect of clonidine and inhibition of noradrenaline release from peripheral pre-junctional nerve endings[3,4,9].

Conclusion

The results of our study correlate with most of the earlier studies. Premedication with oral clonidine 150 µg, 1 hour prior to spinal anesthesia is adequate to provide clinically useful prolongation of sensory blockade without significant adverse effects. However prolonged motor blockade can be uncomfortable for patients. The mechanism whereby oral clonidine may affect spinal anesthesia is unclear. Oral clonidine may exert its effects within the CNS, at peripheral nerve roots, or by potentiation of effects of local anesthetics. Because we did not explore mechanisms of action, our study did not determine whether effects of oral clonidine on spinal anesthesia occurred within the CNS or within peripheral nerves. Thus, further studies are recommended to determine exact sites of action of oral clonidine on spinal anesthesia. Further studies with reference to postoperative analgesic requirements and sedation score are recommended.

Conflict of interest: Nil

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Ethical approval: Obtained

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