

Comparative Evaluation of the Role of 0.5% Hyperbaric Bupivacaine with and without Clonidine under Spinal Anesthesia

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Abstract

Background: Among the various modalities of regional anesthesia, spinal anesthesia is widely practiced. Clonidine is of interest because it preserves cardiovascular reflexes, provides sedation, greater intra operative haemodynamic stability and a reduction in anaesthetic and postoperative analgesics requirements and also has a marked opioid sparing effect. This study was carried out to compare the hemodynamic parameters between 0.5% hyperbaric Bupivacaine with and without Clonidine at various doses. **Methods:** This double blind randomized controlled trial was carried out in a total of 60 patients of age group 20 to 60 years of ASA grade I and II undergoing gynaecological and other lower abdominal surgery under spinal anesthesia. The control group consisted of 15 mg 0.5% hyperbaric bupivacaine while the experimental group was further classified into three groups based on the additional dosage of Clonidine. Presence of hypotension and bradycardia was documented. **Results:** Bradycardia was present in 73.3% of the participants in group IV while it was nil in Group I (controls). Hypotension was present in 73.3% of the participants in group IV while it was absent in group I participants. There was a statistically significant difference in the hypotension between group I & III, I & IV and II & IV ($p < 0.05$). **Conclusion:** our study demonstrates that intrathecal clonidine at the usual dose of $1\mu\text{g}/\text{kg}$ is associated with bradycardia and relative hypotension. Therefore, $0.75\mu\text{g}/\text{Kg}$ of clonidine is the preferred dose for addition to 0.5% hyperbaric bupivacaine in patients undergoing gynaecological and lower abdominal surgeries.

Keywords: Bradycardia; Clonidine; Hyperbaric bupivacaine; Hypotension; Spinal anesthesia.

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Introduction

Regional anesthesia has been advantageous to patients, surgeons and anaesthesiologists alike for many years now due to the simplicity of the method, preservation of consciousness, avoidance of airway instrumentation and rapid recovery

with significant postoperative analgesia.¹ Among the various modalities of regional anesthesia, spinal anesthesia is widely practised because of its technical simplicity and a high success rate. It is a central neuraxial block in which drugs are injected into the subarachnoid space to produce sympathetic, sensory and motor block. It has the advantage of minimal systemic absorption of drugs

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as compared to the drugs injected intravenously resulting in less physiological disturbances and negligible systemic side effects.

Although Lidocaine (Lignocaine), a synthetic local anaesthetic had been widely used due to its safety and popularity, recent studies have examined its effects on transient neurological symptoms following its use for subarachnoid block.² However, Bupivacaine has increased potency over lignocaine and is commonly used as local anaesthetic for spinal anesthesia although its duration of action is shorter.²

A number of drugs e.g. opioids, benzodiazepines, neostigmine and ketamine have been used intrathecally as an adjuvant to local anaesthetics.³ The purpose of combining adjuvants with local anaesthetics is to lower dose of each agent, improve analgesic efficacy and reduce the severity of side effects. Most commonly used intrathecal adjuvants are opioids. They improve the quality of intraoperative analgesia and prolong the postoperative analgesia without significant motor or autonomic blockade. However, side effects such as pruritus, nausea and vomiting, urinary retention and delayed respiratory depression have prompted further research towards non-opioid analgesics with less serious side effects.

Clonidine is known to increase both sensory and motor blockade of local anaesthetics.⁴ Intrathecal clonidine has been used as an adjuvant to local anaesthetics in various surgical procedures without any clinically significant side effects.⁵ Clonidine is of interest because it preserves cardiovascular reflexes, provides sedation, greater intra operative haemodynamic stability and a reduction in anaesthetic and postoperative analgesics requirements and also has a marked opioid sparing effect. Moreover, intrathecal clonidine also prolongs the duration of hyperbaric bupivacaine spinal block.^{6,7} Previous studies have described the use of clonidine in a wide range (15 µg–150 µg). However, the dose response relationship of using clonidine as an adjuvant is less explored. An insight into the role of Clonidine as adjuvant will help in achieving effective regional anesthesia with minimal adverse effects.

The present study is to assess the haemodynamic response and post operative analgesia provided by low dose (0.5, 0.75, 1.0 µg/kg body weight) intrathecal clonidine admixed with 0.5% hyperbaric bupivacaine as compared to 0.5% hyperbaric bupivacaine alone in patients undergoing gynaecological and other lower abdominal surgeries.

Objectives

This study was carried out to compare the hemodynamic parameters between 0.5% hyperbaric Bupivacaine with and without Clonidine at various doses.

Materials and Methods

Study setting and participants

This double blind randomized controlled trial was carried out in the Department of Anaesthesiology of a tertiary teaching institution for a period of four months. A total of 60 patients of age group 20 to 60 yrs of ASA grade I and II undergoing gynaecological and other lower abdominal surgery under spinal anesthesia were selected for the study.

Exclusion criteria

- Patients with spine abnormalities
- Presence of skin infection or local cellulitis.
- Presence of systemic disorders including cardiovascular, neurological, hematological and coagulation disorders.

Randomization

The participants were randomized into

Group I (control group) (15 mg of 0.5% hyperbaric bupivacaine)

Group II (Study Group): 15 mg of 0.5% hyperbaric bupivacaine + clonidine (0.5 µg/kg)

Group III (Study Group): 15 mg of 0.5% hyperbaric bupivacaine + Clonidine (0.75 µg/kg)

Group IV (Study Group): 15 mg of 0.5% hyperbaric bupivacaine + Clonidine (1 µg/kg)

Randomization was carried out using computer generated random numbers.

Sample size and sampling technique

All the patients who underwent elective surgical procedure under spinal anesthesia and were selected through the selection criteria participated in the study. A total of 60 patients were selected and were randomized into four treatment groups, with 15 participants in each group.

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.

Data collection

Pre anaesthetic work up was carried out on all the participants. All the participants received T. Alprazolam 0.25 mg premedication on the day of surgery. In the operation theatre, the baseline pulse rate and blood pressure was recorded on all the participants. Before the subarachnoid block, preloading was done with 20 ml/kg of Ringer Lactate solution.

Procedure

On positioning the patients in lateral decubitus or sitting position, under complete aseptic precautions, lumbar puncture was performed with a 25 gauge Quincke's spinal needle. After ensuring free flow of CSF patients in control group were injected with 15 mg of 0.5% hyperbaric bupivacaine and patients in study group were injected with 15 mg of 0.5% hyperbaric bupivacaine with clonidine 0.5 µg/kg, 0.75 µg/kg and 1 µg/kg according to the groups. The total volume of solution to be injected intrathecally was adjusted to 3.5 ml by adding normal saline. Immediately after injecting the drug the patients were turned supine and oxygen was administered. The following data was recorded during the course of anesthesia –

1. Intra operative monitoring of blood pressure every five minutes for 30 minutes followed by every 15 minutes till the completion of surgery.
2. Total dose of analgesia
3. Duration of surgery.

Operational definitions

Hypotension was defined as fall in systolic blood pressure more than 20% of baseline value or systolic blood pressure less than 90 mm of Hg in the first 20-30 minutes after giving the block. Bradycardia was defined as pulse rate less than 60 per minute. Hypotension was treated with rapid administration of intravenous fluids and use of vasopressors (injection mephentermine 3 mg iv) if needed. Supplemental oxygen was given to every patient through venti-mask during the surgery.

Data analysis

Data was entered and analyzed using SPSS ver. 20 software. Descriptive statistics were expressed in

percentages. Mean scores of sedation and grades of motor blockade were compared with background characteristic using Independent sample t test and chi square test respectively. A *p* value <0.05 was considered statistically significant.

Results

This study was carried out a total of 60 participants, with 15 in each group. The mean age of the participants was similar in all the four groups with mean values ranging from 39.27 to 41.73 years. Similarly, the average weight of the participants was similar among the four groups, ranging from 53.33 to 57.33 kgs. (Table 1) Majority of the participants were females in all the four groups. (Fig. 1) The mean duration of surgery was highest among the controls (Group I), wherein the surgeries last for an average of 130 minutes (Fig. 2).

Heart rate was measured and evaluated throughout the course of surgery for all the four groups. Bradycardia was present in 73.3% of the participants in group IV while it was nil in Group I (controls). (Table 2) We observed a statistically significant correlation with respect to bradycardia between Group IV and all the other groups. The observed difference was statistically significant (*p*<0.005) (Table 3).

Systolic and diastolic blood pressure was recorded from the baseline throughout the surgery and hypotension was identified. Hypotension was present in 73.3% of the participants in group IV while it was absent in group I participants. (Table 4) There was a statistically significant difference in the hypotension between group I & III, I & IV and II & IV (*p*<0.05) (Table 5).

Table 1: Background characteristic of the study participants

S. No	Characteristic	No of patients	Mean ± S.D	Range	
1	Age	I	15	41.73 ± 11.16	25-60
		II	15	40.73 ± 7.27	30-60
		III	15	39.27 ± 10.09	21-60
		IV	15	39.67 ± 11.39	16-56
2	Weight	I	15	55.67 ± 4.95	50-65
		II	15	57.33 ± 4.58	50-60
		III	15	53.33 ± 4.88	50-60
		IV	15	56.00 ± 5.07	50-60

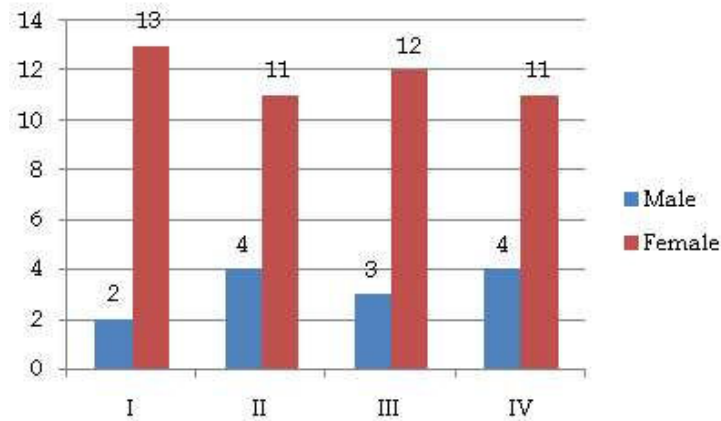


Fig. 1: Gender distribution among the participants:

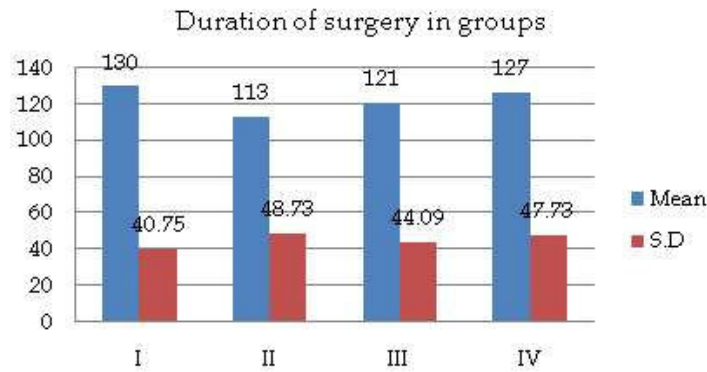


Fig. 2: Mean duration of surgery among all the groups

Table 2: Number of patients having bradycardia (HR <60 bpm)

S. No	Characteristic	Groups							
		I	(%)	II	(%)	III	(%)	IV	(%)
1	Bradycardia								
	Yes	0	0.0	2	13.3	4	(26.7)	11	(73.3)
	No	15	100.0	13	86.7	11	(73.3)	4	(26.7)

Table 3: Association between groups for Bradycardia and hypotension

S. No	Characteristic	Chi Sq	p
1	Bradycardia Groups		
	I vs IV	12.57	0.0001
	II vs IV	13.67	0.003
	III vs IV	7.52	0.027

Table 4: Number of patients having hypotension

S. No	Characteristic	Groups							
		I	(%)	II	(%)	III	(%)	IV	(%)
1	Hypotension								
	Yes	0	0	2	13.33	5	33.33	11	73.33
	No	15	100.0	13	86.67	10	66.67	14	26.67

Table 5: Association between groups for hypotension

S. No	Characteristic	Chi Sq	p
1	Hypotension group		
	I vs III	8.15	0.042
	I vs IV	12.37	0.0001
	II vs IV	16.17	0.003

Discussion

Spinal anesthesia is widely practised for surgeries of lower abdomen and lower limb of body because of its technical simplicity and a high success rate. Local anaesthetics are the most common agents used for this purpose but they are associated with short duration of action and thus requiring analgesic intervention in the early postoperative period. To enhance and prolong the effect of local anaesthetics and reduce their side effects many drugs have been used intrathecally in combination with local anaesthetics. These drugs are called as adjuvants.

Clonidine (a selective partial α_2 adrenergic agonist) has been used as an adjuvant to local anaesthetics intrathecally in various surgical procedures without any clinically significant side effects. Earlier studies have described the use of clonidine in a wide range (15-150 μg). However, the best regimen remains unknown.

In the present randomized, double blind study, there was a significant difference in the mean heart rate and blood pressure between control and experimental group, after 15 minutes of initiation of anesthesia. Similar statistical significance was observed with all the three experimental groups, from the 15th minute onwards in comparison with controls ($p < 0.05$). Our findings were in consonance with the study by P.S. Shetty *et al.* 2006.³ Similar results were shown by Grandhe *et al.* 2008.⁸ Clonidine is known to exert its hemodynamic effects by acting at several sites, either in the central nervous system or in the periphery. Clonidine decreases the heart rate by a presynaptic mediated inhibition of nor-epinephrine release and by direct suppression of atrioventricular node after systemic absorption. The potential for hypotension after spinal clonidine has been noted.

The hemodynamic effects of clonidine are complex and depend on factors such as plasma concentration, route of administration and presence and absence of anesthesia. It has been demonstrated that intrathecal clonidine has depressed effect on systemic blood pressure, mediated by spinal α_2 adreno receptors. Similar results were shown by Kriton *et al.* 1992⁹ It was also observed that the diastolic arterial pressure decreased significantly after intrathecal clonidine compared to control group from 15 to 120 min. Our observations were similar to several published studies.^{10,3,8}

Conclusion

The number of participants who developed hypotension was increasingly higher in the experimental groups compared to the control groups and this was statistically significant. A higher dose of Clonidine attributed heavily to the development of hemodynamic changes. In conclusion our study demonstrates that intrathecal clonidine at the usual dose of 1 $\mu\text{g}/\text{kg}$ is associated with bradycardia and relative hypotension. Therefore, 0.75 $\mu\text{g}/\text{Kg}$ of clonidine is the preferred dose for addition to 0.5% hyperbaric bupivacaine in patients undergoing gynaecological and lower abdominal surgeries.

Conflict of interest: Nil

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