Original Article

Randomized Controlled Trial Using Ropivacaine in Spinal Anesthesia with and without Intravenous Dexmedetomidine in Lower Limb Surgeries

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Abstract

Background: hyperbaric bupivacaine is commonly used in regional anesthesia, especially for the subarachnoid blockade. Several studies demonstrated the efficacy of ropivacaine in different regional anesthesia techniques. Dexmedetomidine has been studied and shown to have synergism local anesthetics. In this study, we aimed to find the efficacy of dexmedetomidine in improving the analgesia quality and duration of the subarachnoid blockade in our hospital scenario.

Materials and Methods: One hundred adult patients were divided into two groups of 50 each. Group A received 3 mL of 0.5% isobaric ropivacaine. Group B received 3 mL 0.5% isobaric ropivacaine was used for spinal anesthesia followed by a loading dose of IV dexmedetomidine. Group A received isotonic saline infusion.

Results: The duration of the motor block in group A was 139.38±21.22 minutes vs.179.13±31.18 minutes in group B ($P<0.05$). Duration of the sensory block in group A was 156.79 ± 33.00 minutes vs. 208.13±48.32 minutes in group B ($P<0.05$), and the duration of the analgesia in group A was 168.69 ± 41.18 minutes vs. 278.57±34.65 minutes in group B ($P<0.05$).

Conclusion: The use of IV dexmedetomidine improves analgesia quality and prolongs anesthesia duration in the subarachnoid block with 0.5% isobaric ropivacaine without any hemodynamic instability and with adequate sedation.

Keywords: Spinal anesthesia, Ropivacaine, Dexmedetomidine, Postoperative analgesia

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Introduction

Spinal anesthesia is a common procedure carried out in the operation theatre and is carried out by injecting a local anesthetic solution into the cerebrospinal fluid in the region of lower lumbar intervertebral spaces. It creates an intense sensory, motor, and sympathetic block and provides excellent operating conditions for surgeries below the dermatomal level of the umbilicus (1, 2). Use of IV dexmedetomidine premedication in general anesthesia has been shown to provide sedation preoperatively, reduces intraoperative inhalational anesthetic requirements, intraoperative, and postoperative analgesia with good hemodynamic stability (3-6). In the central nervous system, the

highest number of alpha 2 adrenoreceptor receptors is present in locus ceruleus, presynaptic activation of theses in locus ceruleus leads to inhibition of noradrenaline release resulting in hypnotic and sedative effects (7-9). In the spinal cord, activation of alpha2 adrenoreceptor receptors at substantia gelatinosa leads to inhibition of nociception and release of substance P (10-12).

Methods

This study was conducted at Sri Siddhartha Medical College Hospital and Research Center, Tumkur (ERC/137/Inst/KR/2013/RR16). CONSORT guidelines were followed in this study. Computer-based randomization was done (The easiest method is simple randomization. If you assign subjects into two groups A and B, you assign subjects to each group purely randomly for every assignment. Even though this is the most basic way, if the total number of samples is small, sample numbers are likely to be assigned unequally. For this reason, we recommend you to use this method when the total number of samples is more than 100). After taking written informed consent, a hundred patients between 20 and 60 years of age, of ASA Class I and II, scheduled for elective lower limb surgeries were enrolled in the study. The investigator and the patient were blinded to the study. A third member of the department was employed to prepare the solutions to be used in the study. Infection at the site of spinal anesthesia, patients with uncontrolled hypertension and diabetes, any neurological or psychiatric diseases, and patients with bleeding or coagulation disorders were excluded from the study.

The following formula was employed to arrive at the sample size.

$$Sample\ size = \frac{z^2 \times (p) \times (1-p)}{c^2}$$

Where:

Z = Z value (e.g. 1.96 for 95% confidence level)

p = percentage picking a choice expressed as a decimal

(.5 used for sample size needed)

c = confidence interval expressed as a decimal

(e.g., .04 = ±4)

The baseline, intraoperative, and postoperative hemodynamic changes at various time intervals were compared between the study groups using Chi-square test and unpaired t-test. Data validation and analysis was carried out by SPSS version 11.0. All the P values < 0.05 were considered significant statistically.

The subjects were randomly allocated using a computer-generated sequence, into either of the groups. Preoperatively all study patients have advised 8 hours' nil per oral. As per the hospital protocols, all patients received Tab. Ranitidine 150 mg orally on the night before surgery at 10 pm also at 5.30 AM with a sip of water as premedication. The patients were transferred to the operation theatre at 8.30 AM. Intravenous access was achieved with an 18G cannula. All patients were preloaded with Ringer's Lactate 10 mL/Kg, 15 minutes before the surgery. In the operating theatre, standard monitoring viz. oxygen saturation (SpO_2) heart rate (HR), non – invasive blood pressure (NIBP), electrocardiogram (ECG) were attached and baseline hemodynamic parameters were recorded. Under aseptic precautions, using a 25G Quincke spinal needle, the subarachnoid block was performed at L_3 – L_4 inter-space in the midline with 0.5% isobaric ropivacaine (Neon Pharmaceuticals, India) was administered at the rate of 0.2 mL/sec.

Group A received 3 mL of 0.5% isobaric ropivacaine and normal saline infusion. Group B received 3 mL 0.5% isobaric ropivacaine, thirty minutes later loading dose of dexmedetomidine 1mcg/Kg was infused over 30 min followed by the maintenance dose of 0.3 mcg/kg/hr IV dexmedetomidine infused till the end of surgery (AKAS Syringe Pump). SpO_2, HR, Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial pressure (MAP) were recorded preoperatively and after performing the subarachnoid block, every 5 minutes till the end of surgery after which they were transferred to the recovery room where they were monitored up to 90 minutes.

Modified Bromage Scale was employed to assess the level of motor block. Time taken for regression of motor block to Modified Bromage Scale 1 was considered. Using pinprick bilaterally at midclavicular line, time of onset of sensory block, level of sensory block, and sensory block duration were recorded. Time taken to reach L5/S1 dermatome was

considered as recovery time for the sensory block. Postoperatively, the Modified Bromage Scale and the sensory level were recorded every 15 minutes until the patients were discharged from the post-anesthesia care unit. The level of pain was assessed by The Visual Analog Scale (VAS). VAS greater than 4 was considered as cut off point to treat pain. IV Paracetamol 1-gram slow infusion was administered for rescue analgesia (13, 14). The level of sedation was assessed by The Ramsay Sedation Score. A score greater than 4 was considered as excessive sedation. Any decrease in MAP of 20% from the baseline was treated with a bolus dose of 6 mg IV ephedrine and infusion of intravenous fluids. HR less than 50/min was treated with IV bolus 0.6 mg atropine. The baseline, intraoperative, and postoperative hemodynamic changes at various time intervals were compared between the study groups using Chi-square test and unpaired t-test. Data validation and analysis was carried out by SPSS Version 16.0. All the P values < 0.05 were considered significant statistically.

Results

The demographic data of the two study groups were comparable (Table 1). Baseline parameters (Table 2) and the mean duration of surgery (Table 3). Both the duration of motor block and sensory block were prolonged in Group B compared to Group A (p<0.001) (Table 4). The two-segment regression in Group A was 74.9±8.64 minutes whereas in Group B it was 99.1±10.79 minutes (P<0.001) (Table 5). The time taken for rescue analgesia was prolonged in Group B compared to Group A (P<0.001) (Table 5). The hemodynamic comparisons are shown in Figures 1 to 7.

In Group A, the mean sedation score was 2 at the beginning of the postoperative period and 1 at the end of 90 minutes whereas in Group B, the mean sedation score was 2.18 at the beginning of the postoperative period and 2.08 at 90 minutes. The Ramsay sedation score was higher in Group B (p<0.05).

In Group A, the VAS score was 2.23 at the beginning of the postoperative period and gradually increased to 4.83 at 90 minutes whereas, in Group B, the VAS score was 0.61 at the beginning of the postoperative period and 2.91 at 90 minutes. The pain scores were higher in Group A (P<0.05). Hence, it is evident from the above observations that intravenous dexmedetomidine administered intraoperatively provides adequate sedation and analgesia that continues even in the postoperative period without causing any respiratory depression.

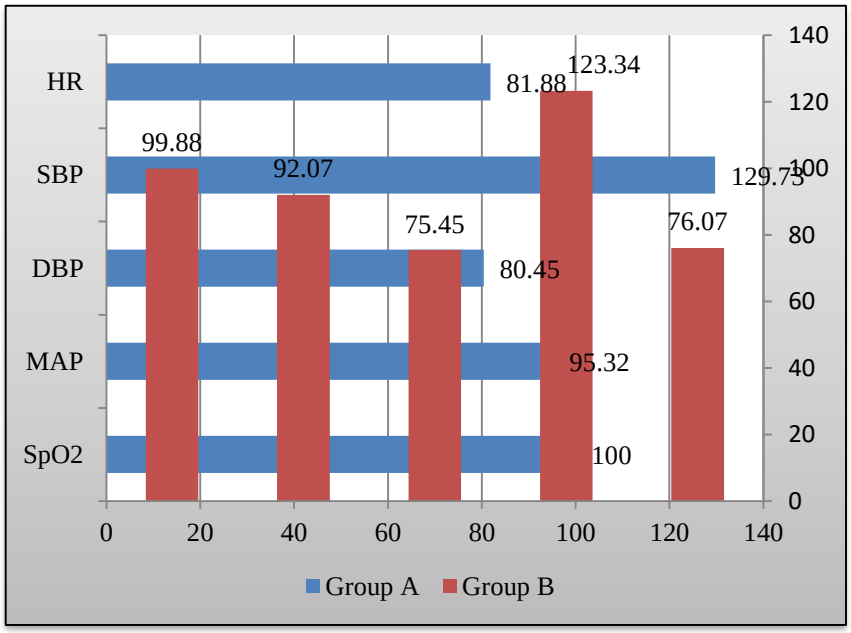

Figure 1: Baseline Hemodynamics.

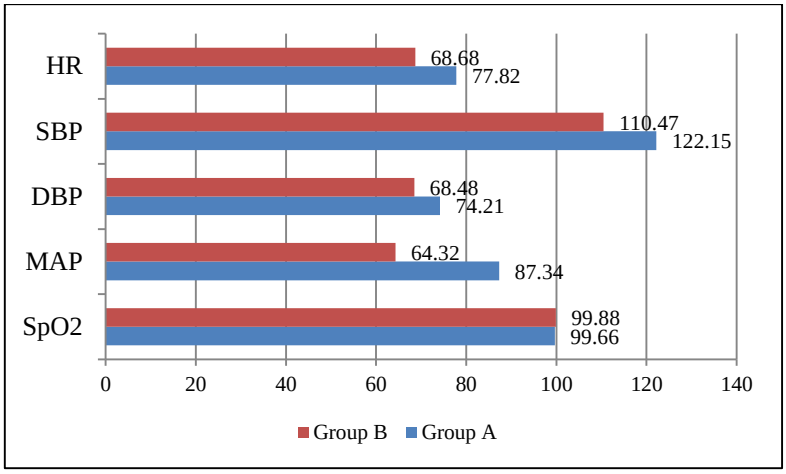

Figure 2: Intraoperative Hemodynamics at various intervals.

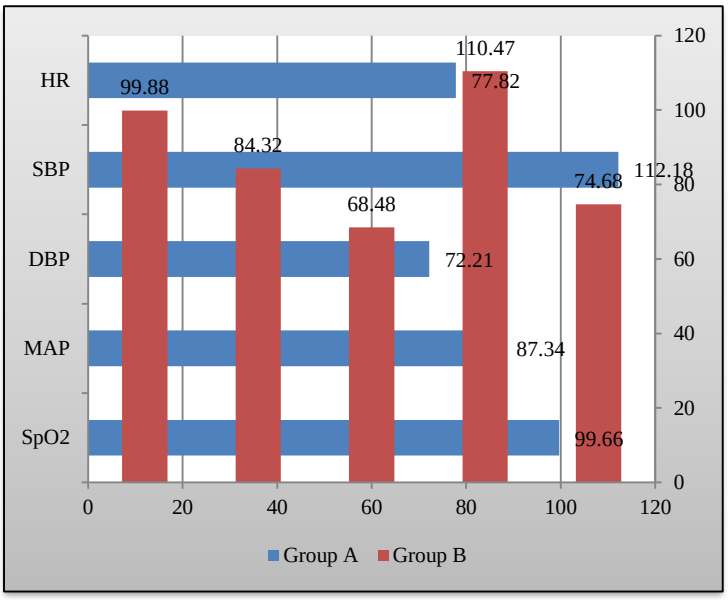

Figure 3: Intraoperative Hemodynamics.

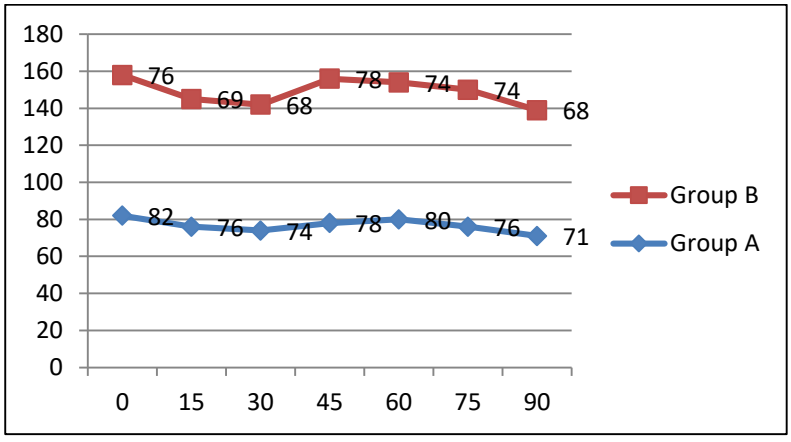

Figure 4: Postoperative HR at various intervals.

Intraoperatively, 7 patients had bradycardia and hypotension in 11 patients in Group A, whereas in

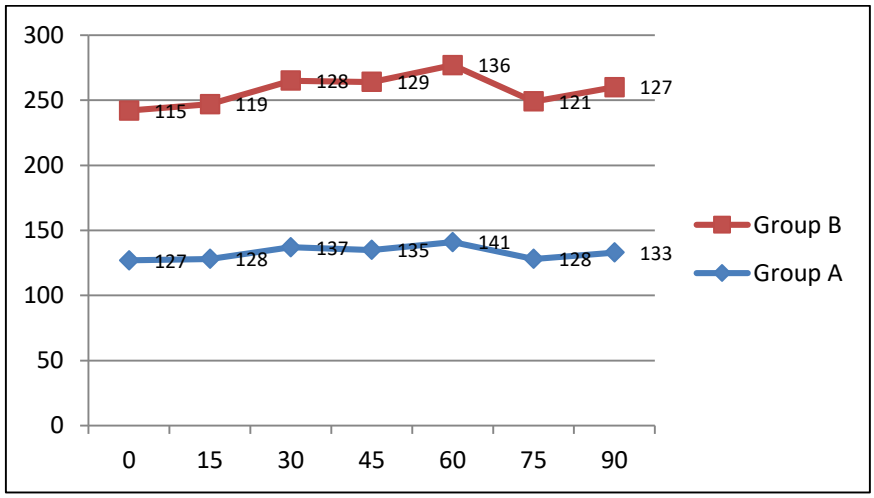

Figure 5: Postoperative SBP at various intervals.

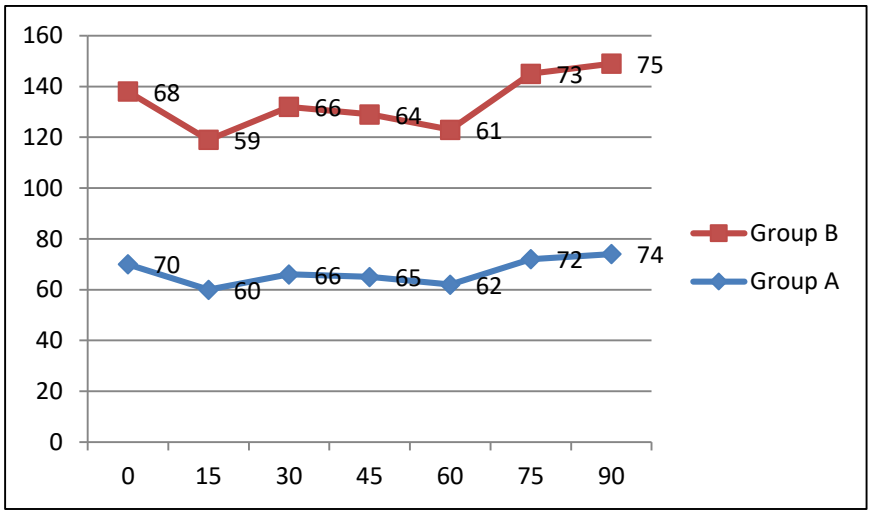

Figure 6: Postoperative DBP at various intervals.

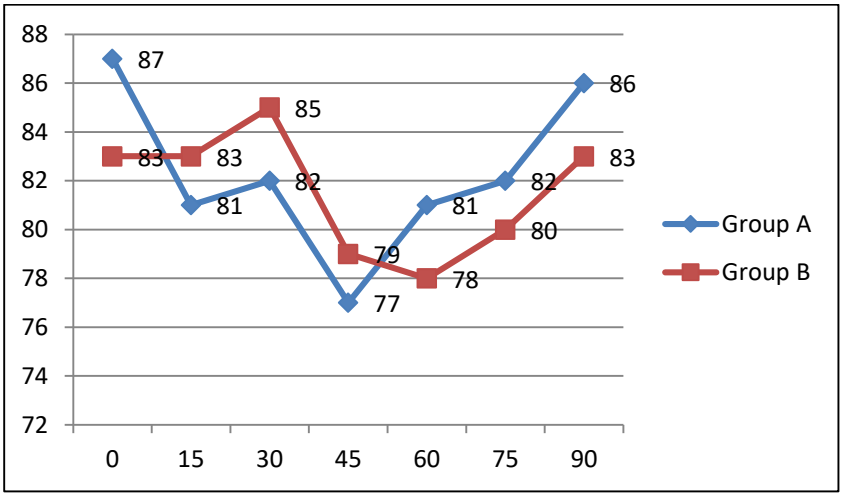

Figure 7: Postoperative MAP at various intervals.

Group B, 3 patients had bradycardia and 3 patients had hypotension. The two groups did not differ

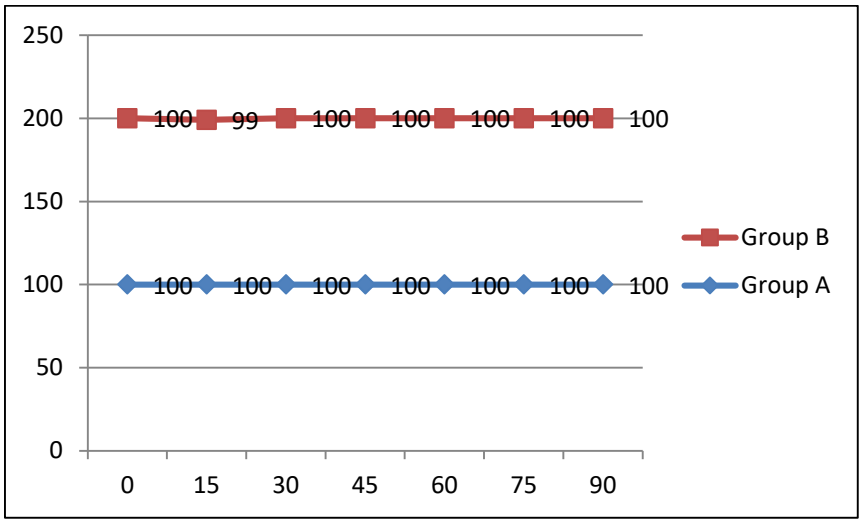

Figure 8. Postoperative SpO_2 at various intervals.

Table 1: Demographic data.

Parameter	Group A	Group B	*p* value
Age (Years)	43.36±7.50	45.31±8.26	0.648
BMI (kg/m^2)	20.24±1.72	19.98±2.11	0.259
Sex (Male/Female)	24:27	23:27	-

Table 2: Baseline Hemodynamic Parameters.

Parameter	Group A	Group B	P value
HR	81.68	76.18	<0.05
SBP	128.73	127.15	<0.05
DBP	76.75	82.44	<0.05
MAP	98.33	96.17	<0.05
SpO_2	100	99.88	<0.05

significantly concerning intraoperative hemodynamics at any interval of time and SpO2 at any time (P>0.05; Figure 8).

In Group A, 1(2%) patient had vomiting whereas, in Group B, none were observed. It was treated with IV Ondansetron 4 mg. In Group A, 1(2%) of patients experienced shivering in the postoperative period. It was treated with IV Pheniramine Maleate 45.5 mg whereas, in Group B, none was observed.

The full Study consort flow diagram is demonstrated in Figure 8.

Discussion

Spinal anesthesia provides good operating conditions for lower abdominal and lower limb surgeries. Many additives and adjuvants have been tried and tested. Intrathecal adjuvants like morphine, fentanyl, sufentanil, neostigmine, ketamine, midazolam, magnesium sulfate, clonidine, and dexmedetomidine, have been used to improve analgesia quality and

Table 3: Duration of Surgery (minutes).

Group A	Group B	P value
97.11±24.79	97.44±26.19	0.95

Table 4: Comparison of sensory and motor blockade (minutes).

Parameter	Group A	Group B	P value
Sensory Blockade	156.79 ± 33.00	. 208.13 ± 48.32	< 0.001
Motor Blockade	139.38 ± 21.22	179.13 ± 31.18	< 0.001

Table 5: Two segment regression (minutes).

Group A	Group B	P value
74.9 ± 8.64	99.1 ± 10.79	< 0.001

anesthesia duration in spinal anesthesia. In a study done by Balwinder Kaur Rekhiet al, it was found that intravenous dexmedetomidine prolonged the effect of ropivacaine (3mg) (15).

In a study done by PDW Fettes et al, plain and hyperbaric solutions of ropivacaine for spinal anesthesia were compared and it was shown that isobaric ropivacaine provided adequate analgesia for lower limb procedures. [16] In a study done by J Chinnappa et al, perineural dexmedetomidine with ropivacaine provided prolonged postoperative analgesia, hastened the onset of sensory and motor block, and prolonged the duration of the supraclavicular brachial plexus block (17).

Ropivacaine causes reversible inhibition of sodium ion influx, and thereby blocks impulse conduction in nerve fibers. This action is potentiated by dose-dependent inhibition of potassium channels. Ropivacaine is less lipophilic than bupivacaine and is less likely to penetrate large myelinated motor fibers; therefore, it has a selective action on the pain – transmitting A, δ, and, C nerves rather than Aβ fibers, which are involved in motor function. Ropivacaine has been shown to inhibit platelet aggregation in plasma at concentrations of 3.75 and 1.88 mg/mL, which correspond to those that, could occur in the epidural space during infusion (18).

Adrenergic receptors were originally differentiated into α and β receptors based on the rank order of potency of various natural and synthetic catecholamines in different physiologic preparations. It was believed that activation of either α- or β-adrenergic receptors produced excitatory effects in some tissues and inhibitory effects in others. Later, a subclass of α adrenoceptor was discovered that regulates the release of neurotransmitters. From this, it was inferred that the receptor is located at the presynaptic site. However, the classification of the receptors based on anatomic location alone is problematic, because $\alpha_2$receptors have also been found at postsynaptic and extrasynaptic sites. Presynaptic α_2 receptors may be of the greatest clinical import because they regulate the release of norepinephrine and adenosine triphosphate through a negative feedback mechanism.

Dexmedetomidine, an imidazole compound, is the pharmacologically active dextranomer of medetomidine that displays specific and selective α_2-adrenoceptor agonists. The mechanism of action is unique and differs from those of currently used sedative agents, including clonidine. Activation of the receptors in the brain and spinal cord inhibits neuronal firing, causing hypotension, bradycardia, sedation, and analgesia. The responses to activation of the receptors in other areas include decreased salivation, decreased secretion, and decreased bowel motility in the gastrointestinal tract; contraction of vascular and other smooth muscle; inhibition of renin release, increased

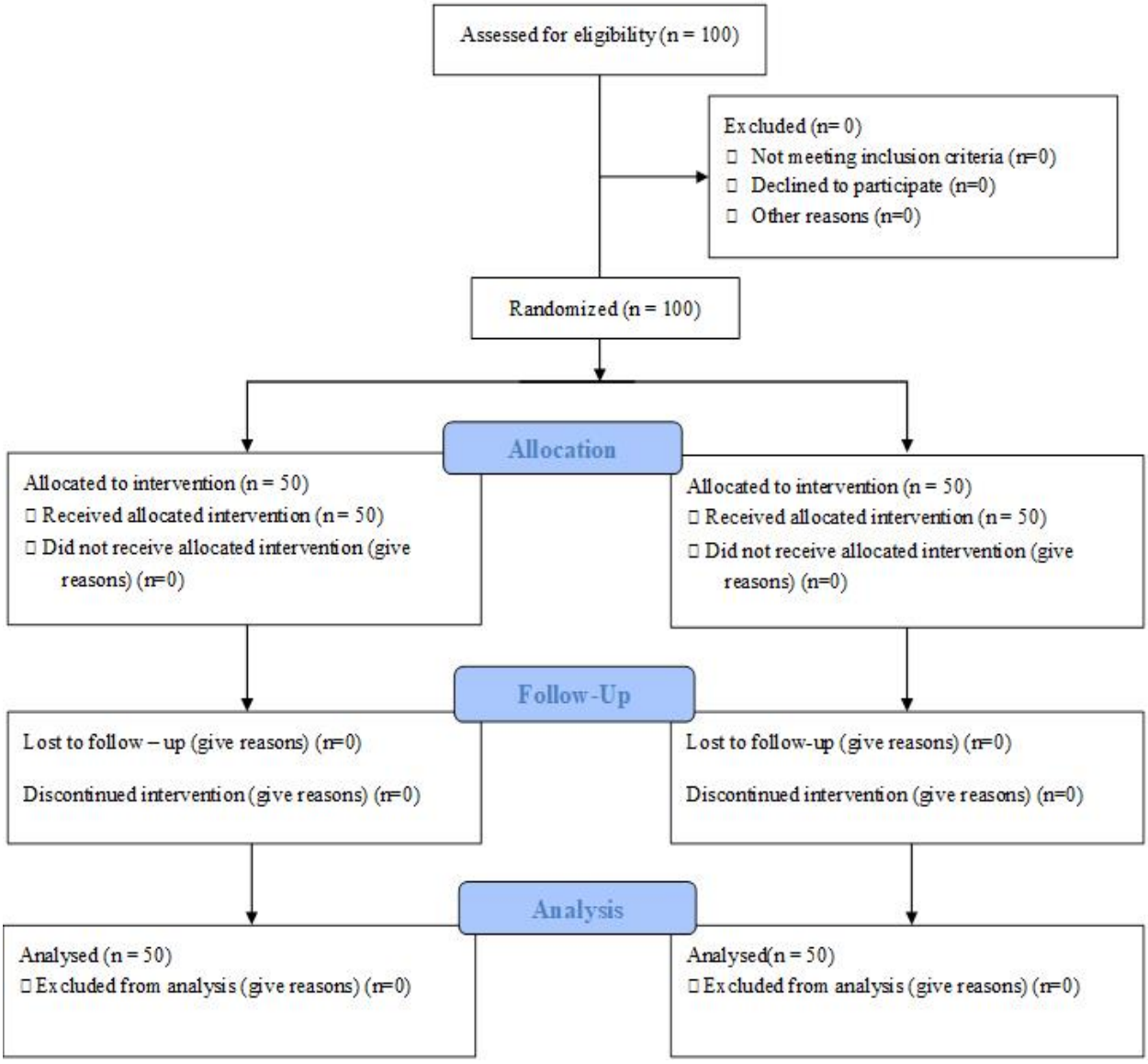

Figure 8: Study consort flow diagram.

glomerular filtration, and increased secretion of sodium and water in the kidney; decreased intraocular pressure, and decreased insulin release from the pancreas (19).

In recent studies, dexmedetomidine has been shown to have a synergistic action with local anesthetics in prolonging the sensory and motor blocks, with good sedation effect and hemodynamic stability. Different adjuvants like opioids, adrenergic agents, GABA agonists, N-Methyl-D-aspartate receptor (NMDA) antagonist, calcium channel antagonist, cholinesterase inhibitors have been used to prolong spinal anesthesia, with reduced postoperative analgesic requirements. Also, these agents help to allay the fear and anxiety of the patient by their sedative effects.

As the study was conducted in a tertiary care center, the people visiting the hospital were of poor socioeconomic and educational status, we found it difficult to accurately explain the nature and purpose of this study. These are inherent problems which were faced by our colleagues in other specialties too. We endeavored to partially overcome this by using simple spoken language and prior explanation to attendees of the subjects.

Conclusion

Ropivacaine has a significantly higher threshold for cardiotoxicity and CNS toxicity than bupivacaine in animals and healthy volunteers and is a good alternative to bupivacaine. The addition of an adjuvant to ropivacaine enhances its safety profile by providing adequate postoperative analgesia.

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Conflicts of Interest

The authors declare and confirm that they have no conflict of interest.

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