

## A comparative study of hyperbaric Ropivacaine with Bupivacaine as spinal anaesthesia

Singhal Rajneesh Kumar<sup>1</sup> and Vyas C.K.<sup>2</sup>

<sup>1</sup>Assistant Professor

<sup>2</sup>Senior Professor, department of Anaesthesia, SMS Medical College And Hospital, Jaipur (Rajasthan) India.

### Abstract:

**Introduction:** Despite off new and excellent inhalational and intravenous anesthetic agents, spinal anesthesia is still a good choice, as it is highly effective both for surgical procedure as well as postoperative pain management and cost effective also. To present study was performed to comparatively evaluate the efficacy of Ropivacaine with Bupivacaine on pain control in terms of duration and intensity of motor block, sensory block and muscle relaxation.

**Material & Methods:** A hospital based prospective, randomized, double blinded and analytical was performed on female patients undergoing cesarean section under spinal anaesthesia in Mahila Chikitsalaya, sanganeri gate, Jaipur. Eighty patients randomly selected and administered hyperbaric solutions of 0.5% Bupivacaine and 0.5% Ropivacaine at the rate of 0.2 ml/sec. Bromage scores, rescue analgesics; motor block, sensory block regression, sedation and nausea were recorded by a blinded observer.

**Results:** There was even distribution of age, weight and height in both the group and mean age, weight and height was not statistically significant in both the groups ( $P > 0.05$ ). No significant differences about onset of anesthesia, vitals, duration of surgical procedures, quality of analgesia and timing of first analgesic intake were found. However, the time to reach T10 sensory block and the time of starting motor block were found to be significantly shorter ( $P < 0.001$ ) in Ropivacaine ( $3.14 \pm 0.58$ ) than Bupivacaine ( $4.4 \pm 0.5$ ). Time to achieve this highest level was also earlier in Bupivacaine ( $8.03 \pm 0.54$ ) than in Ropivacaine ( $11.45 \pm 0.46$ ) ( $P < 0.001$ ). Regression of sensory block to two dermatome ( $68.3 \pm 2.33$  vs  $80.4 \pm 3.32$ ;  $P < 0.001$ ) and duration of sensory block ( $107.6 \pm 6.33$  vs  $128 \pm 6.34$ ;  $P < 0.001$ ) was significantly earlier in Ropivacaine in comparison to Bupivacaine. Patients of both the groups complete motor block and time to achieve complete motor block was significantly shorter in Bupivacaine compared to Ropivacaine ( $6.9 \pm 1.43$  vs  $8.45 \pm 1.06$ ;  $P < 0.001$ ) but recovery of complete motor block or duration of motor block was significantly earlier in Bupivacaine ( $102.75 \pm 12.03$  vs  $146 \pm 18.4$ ;  $P < 0.001$ ). Although Bupivacaine was found to be more potent than Ropivacaine the level of intra-operative adverse effects were more prominent in Bupivacaine administered patients.

**Conclusions:** It was concluded that Ropivacaine although was not superior to Bupivacaine but very well comparable to Bupivacaine. Therefore Ropivacaine can also be a good choice as anaesthetic.

**Keywords:** Analgesic, Ropivacaine, Bupivacaine, Postoperative pain management, T10 sensory block, Bromage Score, Demographic, Motor block, Sensory block and

### I. Introduction

Planning for proper postoperative pain management anaesthetic and its dose is an essential component of good anaesthetic practice since the consequences of untreated pain and inadequate anaesthesia can be devastating<sup>1</sup>. Adequate analgesia aids to restore normal functions including ventilation, coughing and mobility, thereby facilitating early rehabilitation and shortened hospital stay<sup>2</sup>. Various options are available for postoperative analgesia.<sup>3</sup> However, spinal and epidural analgesia, wherever possible, using local anaesthetics with or without additives, provides distinct advantages over other modalities.<sup>4</sup> Both Ropivacaine and Bupivacaine belong to amino-amide group of local anaesthetic drugs. These drugs have the same piperidylidide group which was first synthesized in 1957.<sup>5</sup> Although they have same mechanism of action as other local anesthetics, there exist some differences in their structural, physicochemical, pharmacokinetic and pharmacodynamic properties.

Bupivacaine and Ropivacaine are local anaesthetic with long duration of action, available in 0.25%, 0.5%, 0.75% and 1% concentrations and as hyperbaric and glucose free solutions. Bupivacaine is a racemic mixture of two (R and S) enantiomer, however, Ropivacaine is enantiomerically pure (S-enantiomer) of similar class, structurally related to bupivacaine, but with less cardiac toxicity and neurotoxicity.<sup>6</sup> Available data show Ropivacaine to be very suitable for regional anesthesia. It has been tested in dentistry with encouraging results about its duration of action.<sup>7</sup> Bupivacaine and Ropivacaine, like other local anesthetics, prevent transmission of nerve impulses (conduction blockade) by inhibiting passage of sodium ions through ion-selective sodium channels in nerve membrane. Ropivacaine is less lipid soluble than bupivacaine, so clinically it is less potent in

comparison to Bupivacaine at lower doses, such as the ED50 for labor pain analgesia or other epidural or intrathecal administration.<sup>8</sup> Ropivacaine has similar potency to bupivacaine at doses higher than the ED50 for labor pain relief, such as clinically relevant doses for this application or those used for peripheral nerve block in patients undergoing knee or hip surgery.

In order to compare the efficacy of these two analgesics in postoperative pain management the present study was designed to compare hyperbaric Ropivacaine with hyperbaric Bupivacaine in spinal anaesthesia for cesarean section. Both the drugs were compared in terms of onset, duration and intensity of sensory and motor block, duration of analgesia, intra-operative muscle relaxation and postoperative adverse effects.

## II. Materials and Methods

**Source of data and ethical approval:** The present study includes patients' undergone elective cesarean section under spinal anaesthesia in the Mahila Chikitsalaya, sanganeri gate, Jaipur (an attached hospital to SMS Medical College, Jaipur). The approval for the study was obtained from the Ethical Committee of SMS Medical College, Jaipur under Rajasthan University of Health Sciences, Jaipur. Eighty patients undergoing elective cesarean section under spinal anaesthesia were randomly selected for the study considering the following criteria.

**Study design and sample size:** The present study is a hospital based prospective, randomized, comparative, double blind and analytical study. Assuming the mean difference in onset of sensory block between Bupivacaine and Ropivacaine 0.7 minutes with standard deviation  $\pm 1.1$ , the sample size (n) was estimated 40 patients in each group. Group1 [Control group] (n=40) consist of patients received 0.5% hyperbaric bupivacaine (2 ml), Group2 [Study group] (n=40) consist of patients received 0.5% hyperbaric Ropivacaine (3ml).

**Inclusion and exclusion criteria for selecting patients:** Patients of age 25-35 years having height between 150-165 cm, weighing between 50-70 kg, and belonging to ASA grade I or II were selected for the present study. Patients belonging to ASA grade III or IV, history of any chronic disease like hypertension, diabetes mellitus, respiratory disease, psychiatric or cardiac disease, chronic history of headache and backache, spinal deformity or infection at the local site, known history of hypersensitivity to local anaesthetic, with any neurological or neuromuscular disease, bleeding or clotting abnormalities and patients in whom spinal anaesthesia failed and general anaesthesia was required during previous surgery were excluded from the study group.

**Drug preparation:** The hyperbaric Ropivacaine was prepared by mixing 2 ml of 0.75% isobaric Ropivacaine with 1 ml of 20% dextrose. This gave 0.5% concentration of Ropivacaine in this hyperbaric solution. Commercially available 0.5% hyperbaric Bupivacaine was used as the control drug.

**Procedure for administering spinal anaesthesia:** After confirming overnight fasting patient was taken on the operation table. All the monitors connected to the patient included three lead ECG in standard lead-II. Baseline vitals like B.P., pulse rate and respiratory rate were recorded. After securing an 18G i.v. cannula, preloading was done with 10ml/kg Lactated Ringer solution infusion. Now patient was placed in left lateral position, after proper prepping and draping lumbar puncture was performed in this position at L3-L4 interspaced by midline approach with 25G quincke spinal needle under strict aseptic conditions and the drug was given intrathecally at the rate of 0.2 ml/sec according to the allocated group (after confirming free flow of cerebro-spinal fluid). Time of intrathecal injection was noted and considered as zero. After the intrathecal injection patient was turned supine immediately. A pillow was placed under the shoulder and 15° head down tilt was given. The patient was given 4 L/min of oxygen by ventimask. Infusion of ringer lactate started at the rate of 10ml/kg/hr. started. Vitals were checked and noted in every 2 minutes for first 10 minutes then in every 10 minutes in first hour and in every 30 min thereafter. Arterial oxygen saturation and ECG were observed continuously on connected monitors.

**Statistical Analysis:** Results are presented as mean  $\pm$  SD of three independent experiments and differences between two groups were analyzed for statistical significance by student's t test using GraphPad Prism (version 5) software. Differences with  $P < 0.05$  were considered significant.

## III. Results

**Epidural administration of Ropivacaine provided similar demographic and vital observations as that of Bupivacaine:** Eighty female patients undergoing elective cesarean were included in the present study group were randomly divided into two groups, group I was administered 0.5% Bupivacaine (n=40) served as control group, and group was administered 0.5% Ropivacaine (n=40) which served as study group. All the groups were comparable with regards to mean age (Fig 1A), height (Fig 1B) and weight (Fig 1C) distributions and the duration of surgery (Fig 1E), as there was no significant difference ( $P > 0.05$ ) observed between the two groups. Time from induction to skin incision in two groups was also approximately similar (Fig 1D). This helped in alleviating a point of controversy because different demographic data may influence the effect of spinal anaesthesia.

The vital recordings prior to operation and 1 hour 20 minutes post operation in both the groups followed a similar trend in terms of systolic blood pressure, diastolic blood pressure, pulse rate per min and

respiration rate per minute (Fig 1F and 1G) with no significant differences. These observations revealed that demographic and vitals of Ropivacaine are similar to that of Bupivacaine.

**Bupivacaine provided better sensory and motor block than Ropivacaine but with more adverse postoperative effects:** In the present study onset time of sensory block (sensory block at T10 dermatome) was significantly ( $P < 0.001$ ) earlier in Bupivacaine group ( $3.14 \pm 0.58$ ) in comparison to Ropivacaine group ( $4.4 \pm 0.5$ ), and highest level of sensory block varied between T5-T7 dermatome in both groups but mean T6 level was found to be same for both the drugs. Early onset of sensory blockage was observed in Bupivacaine group along with highest block also (Fig 2A). There was a significant early achievement of highest level of sensory block in Bupivacaine group ( $8.03 \pm 0.54$ ) in comparison to Ropivacaine group ( $11.45 \pm 0.46$ ). At the same time, the time of sensory block regression to 2 dermatome & upto T10 dermatome was earlier in Ropivacaine group ( $68.3 \pm 2.33$  &  $107.6 \pm 6.33$ ) in comparison to Bupivacaine group ( $80.4 \pm 3.32$  &  $128 \pm 6.34$ ) as presented in Fig. 2C. Time to achieve complete motor block was earlier in Bupivacaine group ( $6.9 \pm 1.43$ ) as compared to Ropivacaine group ( $8.45 \pm 1.06$ ) (Fig 2B), while time to achieve complete motor recovery was earlier in Ropivacaine group ( $102.75 \pm 12.03$ ) in comparison to Bupivacaine group ( $146 \pm 18.4$ ) (Fig 2D). Quality of intra operative muscle relaxation as experienced by operating surgeon was almost similar in both the groups. There was a significant difference in duration of complete & effective analgesia in between both the groups (Fig 2E). Duration of complete & effective analgesia was shorter in Ropivacaine group ( $125.25 \pm 10.12$ ) than in Bupivacaine group ( $142 \pm 14$ ). However, when intra-operative adverse effect like hypotension, shivering, nausea and bradycardia were compared in Ropivacaine group with Bupivacaine group, it revealed that in Ropivacaine treated group less but non significant ( $P > 0.05$ ) adverse effects were observed as compared to Bupivacaine treated group (Fig 2F).

#### IV. Discussion

The present study encompasses the study of spinal anaesthesia in patients undergoing elective cesarean section in respect to onset and duration of sensory and motor blockade, highest level of sensory block, quality of intra-operative muscle relaxation, duration of complete analgesia & time to first post operative analgesic administration, haemodynamic effects and intra operative & post operative adverse effects. Since Bupivacaine has its own limitations and complications, so Ropivacaine, a new local anaesthetic was a new interesting candidate of choice.<sup>9</sup> Since there is paucity of literature and conflicting reports on intrathecal use of Ropivacaine, we design this hospital based prospective, randomized, comparative, double blind, analytical study to compare hyperbaric ropivacaine with hyperbaric bupivacaine in spinal anaesthesia for cesarean section in terms of clinical efficacy and safety.

We used hyperbaric solutions in our study because hyperbaric solutions enable a smaller dose to be used compared with plain solutions; plain solutions are less reliable for surgery above the L1 dermatome. Therefore, a hyperbaric solution for spinal anesthesia, especially for caesarean section, is considered superior to an isobaric solution. The optimal dosage of spinal Ropivacaine for caesarean section was unknown; therefore we selected 3:2 with isobaric solution of Bupivacaine and Ropivacaine as used for knee arthroscopy.<sup>10</sup> Based on above studies, we used 15 mg of 0.5% hyperbaric Ropivacaine was comparable to 10 mg of 0.5% hyperbaric Bupivacaine for spinal anaesthesia in caesarean section. The doses are chosen little smaller than in Chung CJ et al. study because Indian women are relatively small in height than western women.<sup>11</sup> Further studies, including a dose response study, are required to determine the optimal dose, concentration and baricity of spinal ropivacaine for caesarean delivery.

Onset time of sensory block (sensory block at T10 dermatome) was significantly earlier in Bupivacaine group in comparison to ropivacaine group. Highest level of sensory block vary in between T5-T7 dermatome in both groups but mean T6 level is same with both the drugs. A possible explanation for this observation could be; since Ropivacaine has lesser lipid solubility may cause delay in penetration of large myelinated A-fibers than the more lipid soluble Bupivacaine.<sup>12</sup> However, faster recovery with Ropivacaine in short surgical procedures like caesarean section could be beneficial because it shortens the stay of post anaesthesia care unit after the delivery. Early recovery of motor block also allows mother for early feeding to newborn. Although the patients satisfaction to recovery of motor block was not assessed clinically and objectively in our study, earlier recovery with spinal ropivacaine may be associated with more patient satisfaction. The quality of intra-operative analgesia was quite good in all patients. No patient of any group complained of discomfort on skin incision. In conclusion, 15 mg of 0.5% hyperbaric Ropivacaine produces similar and adequate anaesthesia required for caesarean section as compared to 10 mg of 0.5% of hyperbaric Bupivacaine with shorter duration of sensory and motor block without significant hemodynamic or other disturbances, but care must be taken for choice in long surgical operations.

### V. Conclusion

Ever since ropivacaine was introduced, there has been an interest to evaluate its safety and dose equivalence as compared to bupivacaine. Our study revealed that 15 mg of 0.5% hyperbaric Ropivacaine produces similar and adequate anaesthesia required for cesarean section as compared to 10 mg of 0.5% of hyperbaric Bupivacaine with shorter duration of sensory and motor block without significant hemodynamic or other disturbances. Faster recovery with Ropivacaine in cesarean section shortens the stay of post anaesthesia care unit after the delivery.

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### Competing interests

The authors declare no competing or financial interests.

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**Table 1: Bromage scoring criteria for degree of blocking**

Grade	C r i t e r i a	D e g r e e o f B l o c k
0	Free movement of legs and feet	Nil ( 0 % )
1	Just able to flex knees with free movement of feet or unable to raise extended leg	P a r t i a l ( 3 3 % )
2	Unable to flex knees but with free movement of feet	A l m o s t c o m p l e t e ( 6 6 % )
3	U n a b l e t o m o v e l e g s o r f e e t	C o m p l e t e ( 1 0 0 % )

**Table 2: Visual analogue score (VAS) for post operative pain**

S c o r e	C r i t e r i a
0	N o p a i n
1, 2 & 3	M i l d p a i n
4, 5 & 6	M o d e r a t e p a i n
7, 8 & 9	S e v e r e p a i n
10	I n t o l e r a b l e p a i n

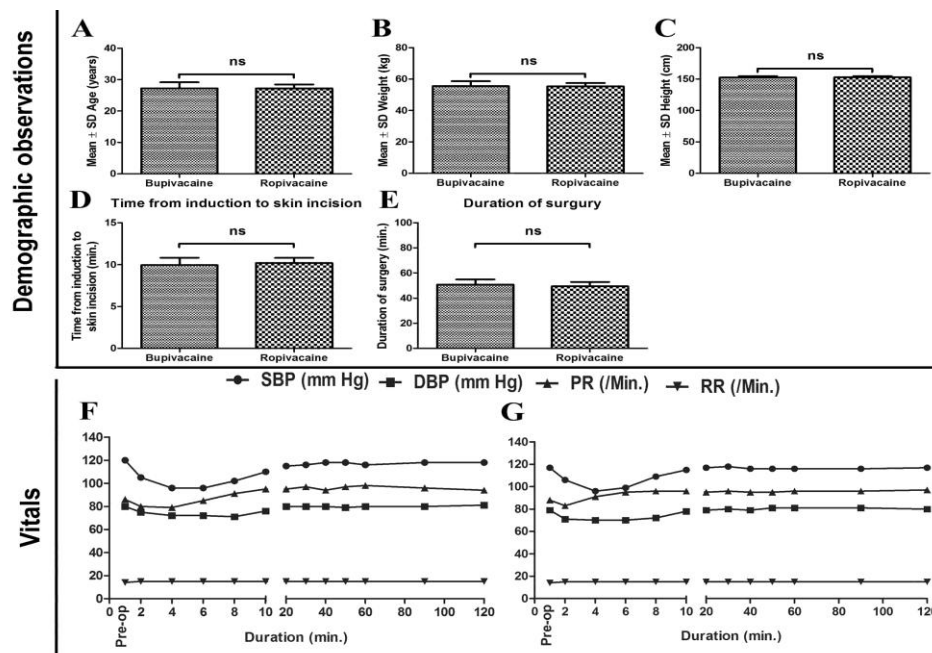


Figure 1

**Figure 1: Pre and post-operative demographic and vital observations in Bupivacaine and Ropivacaine treated patients.** Female patients undergoing elective cesarean were included in the present study group were randomly divided into two groups, group I was administered 0.5% Bupivacaine (n=40) served as control group, and group II was administered 0.5% Ropivacaine (n=40) which served as study group. [A] Mean  $\pm$  SD of age, [B] weight, [C] height, [D] time of induction from skin incision and [E] duration of surgery was recorded in both the anaesthetized groups. Pre-operative and 120 min post operative SBP, DBP, PR/min and RR/min were measured in [F] Bupivacaine and [G] Ropivacaine groups. Data represent the mean  $\pm$  SD. The significance between different experimental groups was calculated by one way ANOVA followed by student's t-test using graph pad Prism (version 5.0) Significance: Bupivacaine and Ropivacaine groups, ns - non significant).

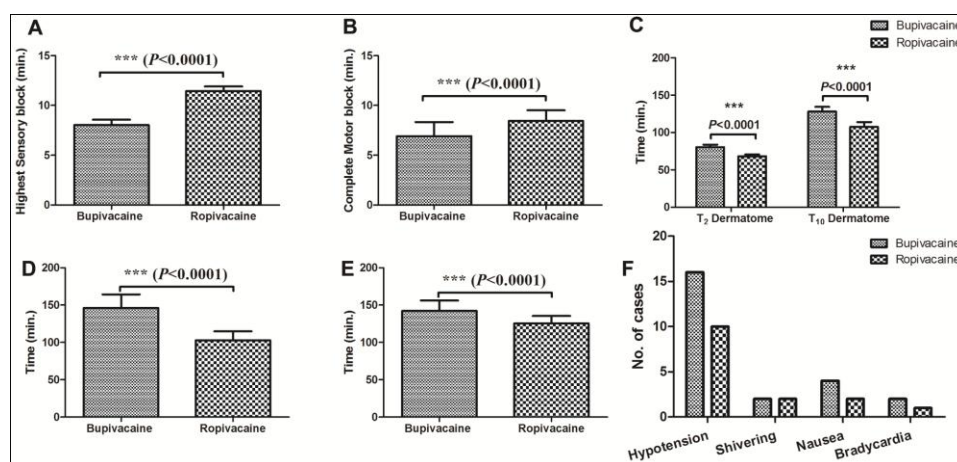


Figure 2

**Figure 2: Comparison of Ropivacaine with Bupivacaine in nerve blocking, regression and intra-operative adverse effects.** Female patients administered with 0.5% Bupivacaine (n=40) and 0.5% Ropivacaine (n=40) were compared for efficacy in pain management, nerve blocking and recovery from anaesthesia. Time taken to achieve complete block and recovery was recorded in each group, and presented as mean  $\pm$  SD. [A] Time taken to achieve highest sensory block. [B] Time taken to achieve complete motor block. [C] T<sub>2</sub> and T<sub>10</sub> Dermatome regression of sensory block. [D] Time taken to achieve complete recovery from motor block. [E] Duration of effective analgesia and [F] Intra-operative adverse effects in two groups. Data represent the mean  $\pm$  SD. The significance between different experimental groups was calculated by one way ANOVA followed by student's t-test using graph pad Prism (version 5.0) Significance: Significance: Bupivacaine and Ropivacaine group \*\*\*p<0.0001.