e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(4); 337-346

Original Research Article

A Comparative Study of Intrathecal Hyperbaric Ropivacaine versus Hyperbaric Bupivacaine for Orthopedic Surgeries

Indranil Halder[1], Uma Mandal[2], Keya Chakraborty[3]

[1]Associate Professor, Department of Pulmonary Medicine, COM & JNM Hospital, Kalyani

[2]Assistant Professor, Department of Anaesthesiology, COM & JNM Hospital, Kalyani

[3]Professor, Department of Anaesthesiology, RKMSP & VIMS, Kolkata

Received: 30-01-2023 / Revised: 28-02-2023 / Accepted: 30-03-2023

Corresponding author: Dr. Keya Chakraborty

Conflict of interest: Nil

Abstract

Background: The clinical effectiveness and safety of hyperbaric ropivacaine and hyperbaric bupivacaine as local anaesthetics for spinal anaesthesia were examined in this study. This investigation was conducted in a tertiary care hospital.

Materials and Methods: 200 patients with ASA physical status of I and II (18–55), scheduled for lower limb orthopaedic procedures under spinal anaesthesia were divided randomly into two equal groups. Group A received 3ml of hyperbaric bupivacaine (0.5%) intrathecally. Group B received 3ml of hyperbaric ropivacaine (0.75%) intrathecally. In the statistical analysis, ANOVA, Paired t-tests, P-value for analytical purposes: 0.05 [95% Confidence Interval] and Chi-square tests were employed. Software for Statistical Analysis was done by MS-Excel/ SPSS/ STATA 14/ R.

Results: The 'Bupivacaine' group significantly outlasted the 'Ropivacaine' group in terms of spinal anaesthetic time, sensory and motor block length, and the time after which the first rescue analgesia was administered. The Bupivacaine group had a significantly lower post-operative VAS score than the Ropivacaine group at 120 minutes, 240 minutes, and 360 minutes.

Conclusions: Intrathecal Inj. of Hyperbaric Ropivacaine (0.75%) 3ml had shorter duration of action than Intrathecal Inj. of Hyperbaric Bupivacaine (0.5%) 3ml but was adequate for the conclusion of the surgery with better perioperative hemodynamic stability than Bupivacaine and could be considered for future use in patients with comorbidities and for early ambulation of post-surgical patients.

Keywords: Analgesia; Spinal Anaesthesia, Hyperbaric Bupivacaine, Hyperbaric Ropivacaine.

Introduction

On August 16, 1898, Professor August Bier conducted the first surgical procedure under spinal anaesthetic at the Royal Surgical Hospital of the University of Kiel, Germany.[1] In the practise of anaesthesia, reducing intraoperative tension and anxiety is

a constant struggle. It also has a number of negative impacts on many bodily systems. Because a lesser dose of local anaesthetic is used, the neuraxial anaesthesia approach is simpler to apply, has a more quick and predictable start, may provide a more severe block, and carries less risk of major systemic drug toxicity. [2-4] One of the most used regional methods is the spinal block. Hyperbaric solutions are a good option for a successful spinal block because they "are more predictable, with greater spread of drug in subarachnoid space in the direction of gravity."[5,6]

Ropivacaine, the S-(-)-enantiomer of 1-propyl-2,6-pipecolo-xylidide, is a brand-new amino-amide local anaesthetic that is structurally linked to bupivacaine and mepivacaine [7] and was created to improve relative sensory and motor block profiles and lower possible toxicity.[8] Hyperbaric ropivacaine has a stereo-selective structure and less lipophilic properties. Compared to Bupivacaine, ropivacaine has a substantially greater threshold for cardiotoxicity and CNS toxicity. The chemical structure of ropivacaine is almost identical to that of bupivacaine, however ropivacaine contains a propyl group on the piperidine nitrogen atom as opposed to bupivacaine, which has a butyl group. In comparison to bupivacaine, ropivacaine has a shorter carbon side chain on the tertiary nitrogen atom. Ropivacaine is less lipid soluble due to its short carbon chain, which affects its potency. [9] Due to less lipophilic property and stereo selective structure Ropivacaine has a significantly higher threshold for cardiotoxicity and CNS toxicity than Bupivacaine.[10,11] Recently, its use as a spinal anaesthetic agent has been evaluated in many procedures because of its equivalent spinal anaesthetic effect and its lower risk of neurotoxicity and cardiotoxicity, compared with bupivacaine and lidocaine.[12,13] To maintain the advantage of an intrathecal anesthetic agent while improving intra- and post-operative analgesia, an analgesic adjuvant can be used.14 Some studies have shown that intrathecal opioids can greatly enhance analgesia from sub therapeutic doses of local anaesthetic.[15-17]

The purpose of this study was to compare the level of adequate block, analgesic efficacy with hemodynamic stability in the intraoperative period, intra and postoperative requirement of rescue analgesia and early ambulation in patients undergoing spinal anesthesia for orthopedic procedures with intrathecal Ropivacaine 3 ml (22.5 mg) and Bupivacaine 3 ml (15mg).

Materials and Methods

On obtaining approval from Institutional ethics committee a prospective randomized comparative interventional study was conducted in the operation theater of RKMSP & VIMS, Kolkata. Written informed consent for examination, participation in the study and undergoing surgery under spinal anaesthesia was taken from all the patients between 18 – 55 years with ASA Physical status I and II, who was scheduled for orthopedic procedures. All investigations were done according to the institutional protocol prior to surgery. Once considered fit for participating in the study selected participants were examined for pre anaesthetic fitness, explained about the procedure and risks of spinal anaesthesia and study, and queries were answered, and routine investigations were checked.Grouping and Randomization: 200 patients were randomly divided into two equal groups. Randomization was done by using double blind simple random sampling by opaque and sealed envelope technique. All the patients were kept fasted as per the fasting guidelines and premedicated with tab Ranitidine 150mg 12hrs prior to surgery. On arrival to the Operation Room, an intravenous access using 18G intravenous cannula was established for all participants. Injection Ondansetron 4mg IV and injection Ranitidine 50mg IV was given 1.5 hours before operation. Preloading was done with 8-10ml/kg of Ringer Lactate over 10-15 mins.

Standard monitors of electrocardiography, pulse oximetry, and noninvasive blood pressure was applied on the non i.v. channeled arm for recording baseline pulse rate, SBP, DBP, MAP, SpO_2, RR. Subarachnoid block was performed following strict aseptic precautions, antiseptic dressing and draping, after anaesthetizing the point of puncture by infiltrating the skin and subcutaneous tissue with Inj. Lignocaine 2% with Adrenaline 1:200000 diluted in equal volume of normal saline by midline approach with the patient in sitting position, using 25G Quincke spinal needle. Group A: Received intrathecal Inj. of hyperbaric Bupivacaine (0.5%) 3ml.Group B: Received intrathecal Inj. of hyperbaric Ropivacaine (0.75%) 3ml. After giving spinal anaesthesia patient was positioned into supine position. The sensory level was assessed by pin-prick sensation using a blunt 25 gauge needle along the midclavicular line bilaterally at 2min, 5mins, 10mins of spinal anesthesia and thereafter at 15 mins interval.

Motor block was assessed by Modified Bromage Scale: Grade 0: no motor loss, Grade 1: inability to flex the hip, Grade 2: inability to flex the knee, Grade 3: inability to flex the ankle. Intraoperative and postoperative hemodynamic monitoring was done. Hypotension (decrease of SBP>20%) was recorded and treated with vasopressor (Inj. Mephentermine) and bolus I.V fluid. Bradycardia (HR<50) was treated with Inj Atropine 0.6mg. Postoperatively in PACU sensory block regression was checked at 30 mins intervals till 2 segment regression from peak sensory level.

Results

1. All the statistical analysis was carried out using Microsoft Excel, 2013 and STATA 14 software.

Motor blockade was assessed till complete regression of motor block of the lower limb. Parameters studied were: Demographic parameters like age (years), weight(kg), and height (cm). Haemodynamic parameters noted were, Systolic blood pressure(SBP), Diastolic blood pressure (DBP), Mean arterial blood pressure(MAP), Heart rate(HR), Respiratory rate (RR) and Peripheral Oxygen saturation (SpO2).

All the above parameters were recorded before giving spinal anesthesia (as baseline), just after giving spinal anaesthesia and then at 3mins interval for first 15mins, at 5 mins interval for 30mins and then at 10mins interval upto the end of the surgery. Postoperatively parameters were recorded at 30 mins interval for 2hrs. Assessment of sensory block was done by noting the onset of sensory block(time required to achieve sensory block up to T10 dermatomal level), peak sensory level, time to achieve peak sensory level, time taken for two segment regression from peak sensory level, duration of spinal anesthesia (when patient complained of pain, VAS 1), time of requirement of first rescue analgesia. Assessment of motor block was done by noting the onset of motor block and the time required for the complete recovery from motor block. VAS score was checked post operatively at 30mins interval for 4 hours.

Any adverse effects such as hypotension, bradycardia, pruritus, nausea and vomiting was recorded. The time of first micturition was noted.

2. Student's t-test was used to test the null hypothesis that the mean of the two groups are same at 5% level of significance.

Demographic Characteristics

Table 1

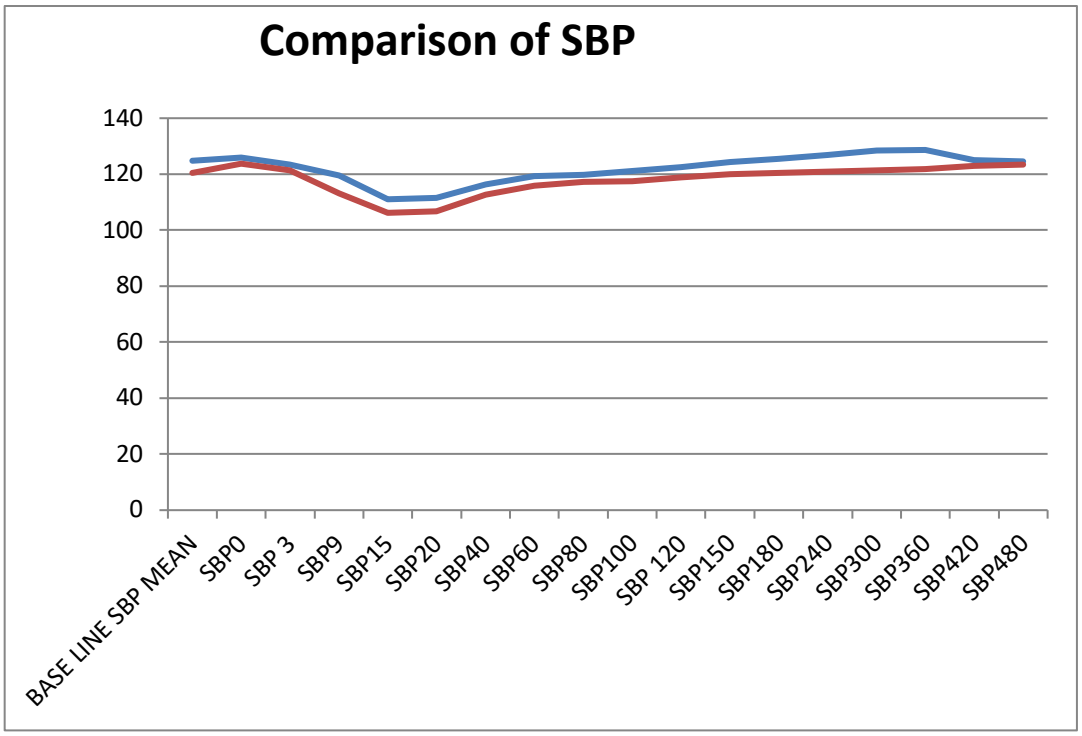
Parameters	Group A : Bupivacaine	Group B : Ropivacaine	p - value
Age (yrs)	46.54 ± 12.26	42.86 ± 13.10	0.15
Height (cms)	63.66 ± 2.39	64.2 ± 2.53	0.27
Weight (kgs)	62.72 ± 5.84	61.46 ± 6.47	0.31
Duration of Surgery (mins.)	108 ± 17.14	110.4 ± 15.38	0.46
Male : Female	28:22	31:19	
ASA PS Grade I : II	25:25	28:22	
SBP (mm Hg)	123.46 ± 5.97	124.76 ± 7.04	0.32
DBP (mm Hg)	78.52 ± 8.24	78.32 ± 6.28	0.89
MAP (mm Hg)	93.44 ± 5.83	93.7 ± 4.72	0.81
HR (bpm)	82.06 ± 9.10	85.58 ± 8.56	0.05

The figures are reported as Mean ± S.D
"p-value < 0.05 is considered significant"

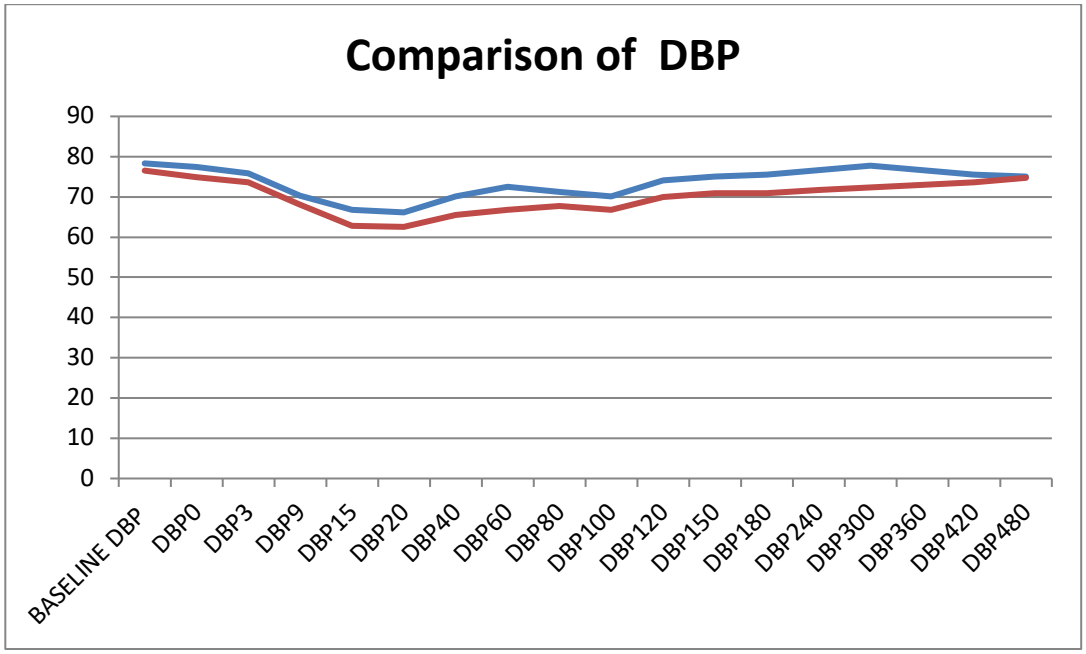
Table 2

	Group A : Bupivacaine	Group B : Ropivacaine	p - value
Onset of sensory block	5.87 ± 1.21	7.49 ± 0.96	0.38
Onset of motor block	8.68 ± 1.27	11.53 ± 1.09	0.48
Time to reach peak sensory level	10.76 ± 0.73	13.04 ± 0.73	0.49
Tme taken for two-segment regression of sensory block	121.78 ± 8.06	96.14 ± 5.20	0.00
Duration of motor block	209.74 ± 10.12	195.86 ± 9.10	0.00
Duration of spinal anaesthesia	246.08 ± 15.53	224.6 ± 6.72	0.00
Time when first rescue analgesia was given	306.82 ± 26.31	245.76 ± 17.31	0.00

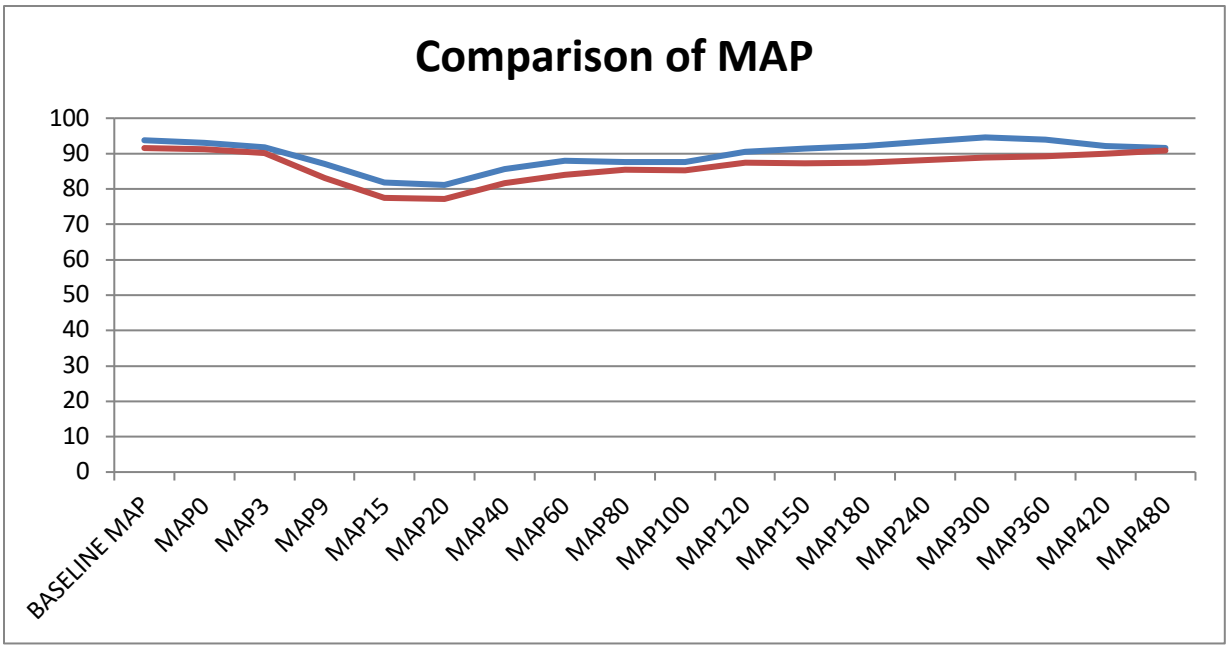
The figures are reported as Mean ± S.D
"p-value < 0.05 is considered significant"



Graph 1: Change in systolic blood pressure
Blue : ROPIVACAINE
Red : BUPIVACAINE



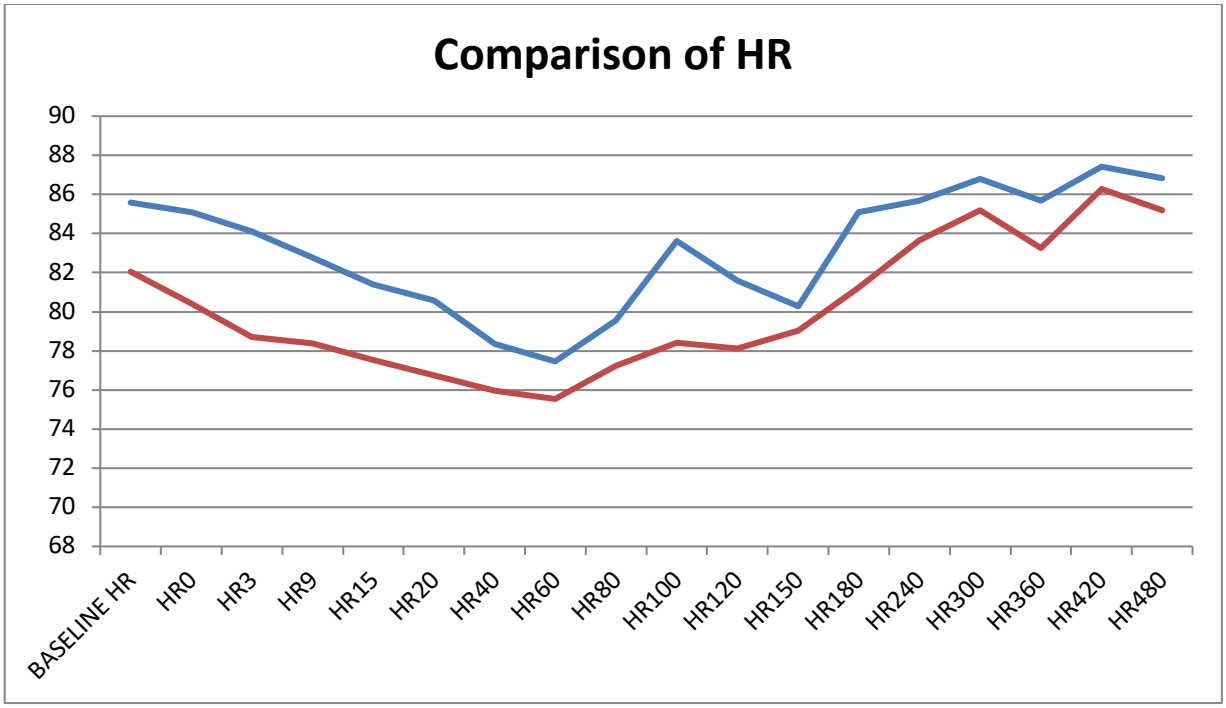
Graph 2: Change in diastolic blood pressure
Blue : ROPIVACAINE
Red : BUPIVACAINE



Graph 3 : Change in mean arterial blood pressure

Blue : ROPIVACAINE

Red : BUPIVACAINE



Graph 4: Change in heart rate

Blue : ROPIVACAINE

Red : BUPIVACAINE

Comparison of VAS Score

Table 3

	Group A : Bupivacaine	Group B : Ropivacaine	p - value
VAS at post-operative 1 min	0	0	
VAS at post-operative 120 mins	0.24 ± 0.43	1.68 ± 0.51	0.00
VAS at post-operative 240 mins	3.42 ± 0.50	4.56 ± 0.50	0.00
VAS at post-operative 360 mins	4.48 ± 0.54	5.54 ± 0.67	0.00
Post-operative Sedation score	1.78 ± 0.46	1.04 ± 0.20	0.00

The figures are reported as Mean ± S.D

"p-value < 0.05 is considered significant"

Discussion

The purpose of the study was to compare the level of adequate block, analgesic effects with haemodynamic stability in the intraoperative phase in patients undergoing spinal anaesthesia for lower limb orthopedic surgeries, comparing the perioperative pain relief, intraoperative haemodynamic stability, intra and postoperative requirement of rescue analgesic and early ambulation between 200 patients,100 in each group. Group A: Received intrathecal Inj. of hyperbaric Bupivacaine (0.5%) 3ml. Group B: Received intrathecal Inj. of hyperbaric Ropivacaine (0.75%) 3ml. The efficacy of the study drug was assessed by the following endpoints: (From Tables 1-3 and Graphs 1-4)

a) T1: ONSET OF SENSORY BLOCK

The 'Bupivacaine' dose had a mean onset time of sensory block of 5.87 minutes whereas the 'Ropivacaine' dose had an onset time of 7.49 minutes. The difference in mean was of 1.62 minute which was insignificant at 5% level of significance with a p-value of 0.38.

b) T2: ONSET OF MOTOR BLOCK

The 'Bupivacaine' dose had a mean onset of 8.68 minutes whereas the 'Ropivacaine' dose has onset of 11.53 minutes. The difference in mean was of 2.85 minutes which was not significant at 5% level of significance with a p-value of 0.48. The difference was both magnitudinally low and statistically insignificant.

c) T3: TIME TO REACH PEAK SENSORY LEVEL

The 'Bupivacaine' dose had a mean time to reach the peak sensory level of 10.76 minutes whereas the 'Ropivacaine' dose had the mean time of 13.04 minutes. The difference in mean was of 0.10 minutes which was insignificant at 5% level of significance with a p-value of 0.49.

d) T4: TME TAKEN FOR TWO-SEGMENT REGRESSION OF SENSORY BLOCK

The 'Bupivacaine' dose had a mean duration of 121.78 minutes whereas the 'Ropivacaine' dose had duration of 96.14 minutes. The difference in mean was of 25.64 minutes which is significant at 5% level of significance with a p-value of 0.00. Though, the duration of sensory block was 96.14 which was lower than the Bupivacaine group but the duration was sufficient to conclude the surgery.

e) T5: DURATION OF MOTOR BLOCK

The 'Bupivacaine' dose had a mean duration of 209.74 minutes whereas the 'Ropivacaine' dose had duration of 195.86 minutes. The difference in mean was of 13.88 minutes which was significant at 5% level of significance with a p-value of 0.00. Though, the duration of motor block was 195.86 minutes which was significantly lower than the Bupivacaine group but the duration was sufficient to conclude the surgery.

f) T6: DURATION OF SPINAL ANAESTHESIA

The 'Bupivacaine' dose had a mean duration of spinal anaesthesia 246.08 minutes whereas the 'Ropivacaine' dose had a duration of 224.06 minutes. The difference in mean was of 21.48 minutes which was significant at 5% level of significance with a p-value of 0.00. Though, the duration of spinal anaesthesia was 224.06 minutes which was significantly lower than the Bupivacaine group but the duration was sufficient to conclude the surgery.

g) T7: TIME WHEN FIRST RESCUE ANALGESIA WAS GIVEN

The 'Bupivacaine' dose had a mean time of 306.82 minutes when the first rescue analgesia was given whereas the 'Ropivacaine' dose had duration of 245.76 minutes. The difference in mean is of 61.06 minutes which was significant at 5% level of significance with a p-value of 0.00. Though, the time when first rescue analgesia was given was 245.76 minutes which was lower than the Ropivacaine group but the duration was sufficient to conclude the surgery.

Mepivacaine, Bupivacaine, and Ropivacaine are three amino-amide local anaesthetics from the pipecoloxylidide family that Ekenstam synthesised in 1957. Only Bupivacaine, though, was created for clinical use among these three local anaesthetics. Up until cases of cardiac arrest linked to its use were disclosed, it was utilised without any knowledge. [18,19] Ropivacaine was produced from the parent chiral chemical Propivacaine as a pure S (-) enantiomer using improved extraction methods and stereoselective synthesis. Enantiomeric purity in its commercial preparation is 99.5%.[20] The chemical structure of ropivacaine is almost identical to that of bupivacaine, however ropivacaine contains a propyl group on the piperidine nitrogen atom as opposed to bupivacaine, which has a butyl group. In comparison to bupivacaine, ropivacaine has a shorter carbon side chain on the tertiary nitrogen atom. The short carbon chain of ropivacaine makes it less lipid soluble, which affects the compound's efficacy.The myelination and size of the nerve fibres are directly correlated with the effects of local anaesthesia. Large myelinated motor fibres can be penetrated by more lipophilic local anaesthetics than by less lipophilic local anaesthetics. However, it is believed that changes in the lipophilicity of local anaesthetic medicines have little bearing on the penetration of tiny unmyelinated sensory A and C fibre.[21] Ropivacaine has selective action on the pain-transmitting A and C nerves rather than A fibres, which are implicated in motor function, since it is less lipophilic and penetrates fewer big myelinated motor fibres. Thus Ropivacaine shows more selective sensory versus motor blockade than the more lipophilic bupivacaine. In a trial involving lower limb surgeries, done by Kallio H. et. al., the duration of sensory block with Ropivacaine 15 mg was found to be similar with bupivacaine 10 mg, and the motor block was significantly shorter. It was also suggested that on a milligram for milligram basis, the potency of Ropivacaine relative to bupivacaine is two-thirds with regard to sensory block and half with regard to motor block. P. D. W. Fettes et.al. did a comparative study of plain and hyperbaric solutions of Ropivacaine for spinal anaesthesia and confirmed that hyperbaric solution of Ropivacaine produces a more consistent block than a plain one.[22] Kalpana R Kulkarni, et.al. did a randomized comparative study to compare the clinical efficacy of equal doses of hyperbaric 0.5% Ropivacaine with 0.5% Bupivacaine, concluded that: "Ropivacaine 15 mg in dextrose 8.3% provides reliable SA of shorter duration than Bupivacaine 15 mg in 8% dextrose. Thus Ropivacaine is 40% less potent than Bupivacaine". Ropivacaine 5mg/ml was made hyperbaric by the addition of dextrose 83 mg/ml. [23] Feroz Ahmad Dar et.al. did prospective study to compare the efficacy and safety of intrathecal 0.5% hyperbaric Ropivacaine 3ml with 0.5%, hyperbaric

bupivacaine 3ml, and concluded that: "The solution of hyperbaric Ropivacaine can be used for spinal anaesthesia and is comparable with hyperbaric bupivacaine in terms of quality of block".[24] J. B Whiteside et.al in their comparative study of Ropivacaine 0.5% (in glucose 5%) with bupivacaine 0.5% (in glucose 8%) for spinal anaesthesia to compare the clinical efficacy of hyperbaric Ropivacaine with that of the commercially available hyperbaric preparation of bupivacaine; concluded that:

"Ropivacaine 15 mg in glucose 50 mg/ ml provides reliable spinal anaesthesia of shorter duration and with less hypotension than bupivacaine." [25]

Conclusion

From the results we concluded that in the study there was no significant difference in the onset of sensory block, onset of motor block and the time to reach the peak sensory level for the 'Ropivacaine' dose as compared to the 'Bupivacaine' dosage. The duration of sensory block, duration of motor block, duration of spinal anaesthesia, the time after which first rescue analgesia was given and the post-operative VAS score were significantly lower for the 'Ropivacaine' doses than the 'Bupivacaine' doses, but it was sufficient to conclude the surgery. Early ambulation was also possible in all the patients postoperatively. Hence we may conclude that Hyperbaric Ropivacaine with better perioperative hemodynamic stability than Hyperbaric Bupivacaine could be considered for future use in patients with co morbidities and for early ambulation of post-surgical patients for better perioperative outcome.

Acknowledgements

The authors would like to thank the hospital authorities and the record section for allowing us to collect the required hospital data and for their excellent technical support in preparing the article.

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