ISSN 2515-8260 Volume 09, Issue 07, 2022

Comparative study of intrathecal 0.42% hyperbaric Levobupivacaine versus 0.42% hyperbaric Ropivacaine for elective infraumbilical surgeries

1.Beladakere Channaiah Vijayalakshmi: Department Of Anaesthesiology, Mysore Medical College and Research Institute, Mysuru- 570001,Karnataka state, India

2.Lakshmipriya: Department Of Anaesthesiology, Mysore Medical College and Research Institute, Mysuru- 570001,Karnataka state, India

3.Mallesh L : Anaesthesiologist, General Hospital, Kanakapura-562117, Karnataka state, India

4.Anand Shalini: Department Of Anaesthesiology, Mysore Medical College and Research Institute, Mysuru- 570001,Karnataka state, India

5.Deepa Palax Kattishettar: Department Of Anaesthesiology, Mysore Medical College and Research Institute, Mysuru- 570001,Karnataka state, India

6.Vinayaka Chatram Shivananda : Dept of Cardiothoracic surgery, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Mysore, Karnataka state,India

Abstract:

***Background and objectives*:** One of the most important determinants affecting the level of anaesthesia after subarachnoid block is the baricity of local anaesthetic. Hyperbaric local anaesthetic solutions are more predictable with greater intrathecal spread and less interpatient variability. This study was designed to compare these two drugs in hyperbaric forms in patients undergoing elective infraumbilical surgeries under spinal anaesthesia.

Materials and methods: 100 patients of either sex, aged between 18 to 60 years and belonging to American society of Anaesthesiologists (ASA) physical status class I and II who were posted for various elective infraumbilical surgeries under spinal anaesthesia were randomly allocated to two groups of 50 each, to receive either 2.5 ml of 0.42% hyperbaric Levobupivacaine (group HL) or 2.5 ml of 0.42% hyperbaric Ropivacaine (group HR) intrathecally. Sensory and motor characteristics, haemodynamic parameters and adverse effects if any were recorded and data analysed with appropriate tests.

Results: There was no statistically significant difference observed between the two groups with regards to mean time for onset of sensory and motor block (4.16±1.06 and 3.56±1.18mins in group HL vs 3.89±1.61 and 7.06± 0.99 mins in group HR). Mean time taken to achieve maximum level of sensory block and motor block were significantly shorter in group HL (7.06±1.33 and 8.81±9.0 mins) compared to group HR (10.13±2.53 and 12.91±1.48 mins). Mean time for two segment sensory regression, sensory level regression to S1, total duration of analgesia and motor block were significantly prolonged in group HL compared to group HR (109.56±12.63 vs 74.80±7.45 mins, 234.88±27.95 vs 163.16± 15.38 mins, 215.22±26.26 vs 148.34±15.73 mins and 158.16±22.7 vs 95.98±14.06 mins respectively).

Interpretation and conclusion: Both hyperbaric Levobupivacaine and hyperbaric Ropivacaine produced reliable and adequate spinal blockade for infraumbilical surgeries without significant hemodynamic changes, however hyperbaric Levobupivacaine produced prolonged sensory and motor blockade compared to hyperbaric Ropivacaine.

Keywords: Hyperbaric Levobupivacaine; Hyperbaric Ropivacaine; Spinal anaesthesia; Infraumbilical surgeries

Introduction:

Subarachnoid block (SAB) is the most widely used anaesthetic technique for infraumbilical surgeries providing a fast onset and effective sensory and motor blockade.[1] A wide variety of local anaesthetic drugs are available for spinal anaesthesia namely Bupivacaine, Levobupivacaine and Ropivacaine. One of the most important physical properties affecting the level of anaesthesia after the intrathecal administration of local anaesthetic is its baricity i.e.density of injectate to density of cerebrospinal fluid (CSF).[2]

Hyperbaric Bupivacaine 0.5% is the most commonly used drug for spinal anaesthesia after the discontinuation of Lidocaine's intrathecal use due to the development of transient neurological symptoms. Hyperbaric Bupivacaine hydrochloride 0.5% is extensively used because of its longer duration of sensory and motor blockade.[3] Bupivacaine is available as a racemic mixture of its enantiomers, Dextrobupivacaine and Levobupivacaine. It has been found that dextro-enantiomer is the cause for cardiotoxicity and the Levobupivacaine (S-1-butyl-2-piperidylformo-2', 6'-xylidide hydrochloride), the pure S (-) enantiomer does not have the cardiotoxicity.

Levobupivacaine is an amide local anaesthetic which was introduced in India in 2012 and is available as 0.5% isobaric solution for intrathecal use with a clinical profile resembling that of Bupivacaine. It has been stated that its faster protein binding rate reflects a decreased degree of toxicity and studies done have supported that it has lesser cardiovascular and central nervous system toxicity than Bupivacaine**.** [4,5,6] A few studies suggest that hyperbaric Levobupivacaine was more predictable for sensory block level and more effective for surgical procedures with lower abdominal approach.[7]

Ropivacaine being a pure S-enantiomer of parent chiral molecule propivacaine belongs to the pipecoloxylidine group of local anaesthetics.[8] It produces similar sensory block to that of an equivalent dose of Bupivacaine with reduced degree of motor block and reduced potential for cardiotoxicity and neurotoxicity. Addition of dextrose to Ropivacaine has proved to increase the speed of onset, block reliability, duration of useful block and speed of recovery.[9]

Use of hyperbaric form of local anaesthetics is popular among many anaesthesiologists in India as their effect is very predictable. Hyperbaric form of both Levobupivacaine and Ropivacaine is not commercially available in India and required to be prepared by adding dextrose and hence it will be interesting to know their effects on spinal anaesthesia. Hence this study was designed to investigate and compare the clinical effects of hyperbaric Levobupivacaine and hyperbaric Ropivacaine on spinal anaesthesia for elective infraumbilical surgeries.

ISSN 2515-8260 Volume 09, Issue 07, 2022

Materials and methods:

A pilot study was conducted on 10 patients receiving either intrathecal 2.5ml of 0.42% Levobupivacaine (83 mg/ml dextrose) or 2.5ml of hyperbaric 0.42% Ropivacaine (83 mg/ml dextrose). Autoclaved ampoules of 50% dextrose were used for each patient to maintain sterility for mixing with commercially available sterile isobaric Levobupivacaine or Ropivacaine for intrathecal use. Samples of hyperbaric 0.42% Levobupivacaine and hyperbaric 0.42% Ropivacaine and (containing dextrose 83 mg/ml) were sent to the laboratory to test the specific gravity and for culture sensitivity. The mean specific gravity of hyperbaric levobupivacaine and hyperbaric ropivacaine were noted (HL-1.0446 and HR-1.0396). The samples were negative for culture sensitivity test.

After institutional ethical committee approval this prospective, double blind, randomized clinical study was conducted on 100 patients of either sex, aged between 18 to 60 years, height 150-175 cms, who gave a valid informed written consent and belonged to American society of Anaesthesiologists (ASA) physical status class I and II and were posted for various elective infraumbilical surgeries at Krishna Rajendra Hospital attached to Mysore Medical College and Research Institute, Mysore.

Patients with systemic diseases like diabetes mellitus, hypertension, cardiovascular, respiratory, hepatic, renal or neurologic disorders, who fall under ASA physical status III and IV, pregnant females, body mass index (BMI) more than 30 kg/m^2, those posted for emergency surgeries were excluded from the study. Unwilling patients, patients with history of known hypersensitivity to study drugs, coagulation abnormalities, local sepsis at the site of lumbar puncture, with deformity of spine and any other contraindication to subarachnoid block were also excluded from the study.

A thorough pre-anaesthetic check-up was carried out for each patient including relevant laboratory and radiological investigations. All patients were visited a day prior to the surgery and explained in detail about the anaesthetic technique. Tablet Ranitidine 150mg and tablet Alprazolam 0.5mg orally were given at night as a pre-medication and patients were kept nil per orally for solids 6 hrs and clear fluids 2 hrs before surgery. On the day of surgery, after securing an intravenous access with 18G cannula patients were preloaded with Ringer lactate solution 10ml/kg before the initiation of spinal anaesthesia.

The data was collected in a pretested proforma meeting the objectives of this study. The study population was randomly divided by shuffled sealed opaque envelope technique into two groups with 50 patients in each group (n=50).

Group HL (n=50): 2.5 ml of 0.42% hyperbaric Levobupivacaine.

Group HR (n=50): 2.5ml of 0.42% hyperbaric Ropivacaine.

Preparation of the drug was done by a senior anaesthesiologist who does the randomization but was not involved further in the study and then the drug was given to the anaesthesiologist who performed spinal anaesthesia and was also an observer. Hence the patient and the observer were blinded to the study drug.

2.5ml of either commercially available sterile preservative free isobaric Levobupivacaine 0.5% (Levo-Anawin, Neon) or isobaric Ropivacaine 0.5% (Ropin, Neon) was loaded in the 5 ml sterile syringe. To this 0.5ml of 50% autoclaved dextrose was added by using insulin syringe. Total 3 ml of study drug would contain 12.5 mg of Levobupivacaine or Ropivacaine and 250 mg of dextrose. Out of 3ml of study drug, 2.5 ml was given intrathecally. Each ml of this study drug would contain 4.2mg of Levobupivacaine or Ropivacaine and 83.33 mg of dextrose.

Monitoring was done using multi-parameter monitor (EDAN IM-80) having pulse-oximetry, electro-cardiography (ECG) and non-invasive blood pressure (NIBP). For spinal anaesthesia patients was placed in lateral decubitus position with table kept flat horizontally. Under aseptic precautions lumbar puncture was performed at the level of L2-L3 or L3-L4 through midline approach using 25G Quincke's spinal needle and prepared study drug either 2.5 ml of sterile 0.42% hyperbaric Levobupivacaine or 2.5ml of sterile 0.42% hyperbaric Ropivacaine was injected into the subarachnoid space after confirmation of free flow of CSF. Patients were made to turn into supine posture immediately after spinal anaesthesia and supplementary oxygen was given with mask.

Time of intrathecal injection was noted. Sensory block was assessed by loss of pinprick sensation to a blunt 27G hypodermic needle every 30 seconds for first 2 minutes(mins), every minute for next 5 mins and every 5 mins for next 15 mins and every 10 mins for next 30 mins and every 15 mins till the end of surgery and there after every 30 mins until sensory block was resolved. Degree of motor block was assessed by using modified Bromage scale [10] (0=none, 1=inability to raise extended leg; able to move knee and feet, 2= inability to raise extended leg and move knee; able to move feet only, 3=complete block of motor limb).

Onset of sensory block was considered as the time taken from intrathecal injection of drug to loss of sensation to pinprick at T10 dermatome. Maximum level of sensory block attained, time taken for maximum dermatomal level, two segment sensory regression time, time for sensory level regression to S1 dermatome were noted. Total duration of analgesia was taken as the time from the completion of the injection of the study drug till the patient requests for rescue analgesic in the post operative period. The time needed for the onset of motor block (Bromage 1), time taken for maximum motor block and total duration of motor block (time taken for complete motor recovery to Bromage 0) were also noted. All durations were calculated considering the time of spinal injection as time zero.

Haemodynamic parameters like heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were monitored every 2 minutes (mins) for the first 10 mins, every 5 mins for the next 30 mins and then every 15 mins till the completion of surgery and perioperative period till complete sensory and motor recovery, employing multi-parameter monitor. IV Mephenteramine 6mg was given to treat arterial hypotension (reduction in Systolic Blood Pressure (SBP) > 20% from basal value or SBP <90 mm of Hg) and inj. Atropine administered if pulse rate went below 55 beats per min (bpm).

Statistical analysis:

Sample size calculation was based on previous studies. An estimated 45 patients per group were necessary in order to detect at-least clinically significant difference of 30 mins in mean duration of analgesia between the groups for achieving type 1 error of 0.05 with 80% power and 95% confidence interval for group comparison. To compensate for the dropout from the study and also to make sure that the sampling size is adequate, a total number of 100 subjects were selected.

Continuous variables were summarized in the form of mean ± standard deviation (SD), median (range) and categorical variables as percentages. The results were analysed statistically using student's t-test **(**for continuous variables) and Chi-square test (for categorical variables). All variables are presented in the form of tables and graphs

Data were entered in a spreadsheet and then exported to data editor of Statistical Package for Social Sciences (SPSS; Windows Ver 22.0) for analysis. p value < 0.05 was deemed to be significant and <0.01 as highly significant.

Results:

The two groups of patients enrolled in the study did not differ significantly with respect to age, sex, body weight, height, ASA status and duration of surgery as shown in Table1.

Table 1: Showing demographic characteristics (Mean ± SD)

Demographic criteria	**Group HL**	**Group HR**	**p value**
Mean age (in yrs)	42.24±12.3	42.48±11.64	0.656(NS)
Sex (male /female)	25/25	26/24	0.841 (NS)
Weight (in Kgs)	57.22±4.85	56.84 ± 4.19	0.676(NS)
Height (in cms)	159.26±4.39	159.58 ±3.70	0.695(NS)
BMI (kg/m^2)	22.56±1.64	22.33±1.55	0.467(NS)
ASA 1 / 2	25/25	25/25	1.0 (NS)
Duration of surgery (in mins)	79.20 ± 8.71	79.60 ± 8.08	0.812 (NS)

NS- not significant (p>0.05)

The salient features regarding sensory and motor block characteristics in both the groups are tabulated in tables 2 and 3 respectively.

Table 2: Sensory block characteristics (Mean ± SD)

	Group HL	**Group HR**	**p value**
Onset time of sensory block at T10 (in mins)	4.17 ± 1.06	3.89 ± 1.61	0.308 (NS)
Maximal dermatomal level achieved T4/T6/T8/T10 (in number)	4/13/20/13	3/11/22/14	0.666(NS)

Time to achieve maximum dermatomal level (in mins)	7.05 ±1.33	10.13±2.53	<0.001(HS)
Time for two segment sensory level regression (in mins)	109.56 ±12.63	74.80 ±7.45	<0.001(HS)
Time for sensory regression to S1 (in mins)	234.88±27.96	163.16± 15.38	<0.001(HS)
Total duration of analgesia (in mins)	215.22 ±26.26	148.34 ± 15.74	<0.001(HS)

HS-Highly significant($p<0.01$); NS- not significant ($p>0.05$)

Table 3: Characteristics of motor blockade (Mean ± SD)

	Group HL	**Group HR**	**p value**
Time taken for onset (Bromage 1) (in mins)	3.56 ±1.13	7.06± 0.99	<0.001(HS)
Grade of motor block achieved Bromage 0/1/2/3 (in number)	0/0/16/34	0/0/22/28	0.216(NS)
Time taken to achieve complete motor block (in mins)	8.81 ± 9.00	12.91 ±1.48	0.002(HS)
Total duration of motor block (in mins)	158.16 ±22.76	95.98±14.06	<0.001(HS)

HS-Highly significant($p<0.01$), NS- not significant ($p>0.05$)

In our study time to achieve T10 dermatomal level of analgesia was faster in group HR (3.89 ± 1.61 mins) when compared to group HL (4.17 ± 1.06 mins) which was statistically insignificant ($p>0.05$). The maximum sensory level achieved in both the groups were comparable and statistically not significant ($p= 0.666$). Maximum level of sensory analgesia in Group HL was T4 and Group HR was also T4. Hence the mean level of sensory analgesia was T 7.2±1.71(T4-T10) in HL group and T 7.4±1.61(T4-T10) in HR group. The time taken to achieve this maximum sensory level was significantly faster in group HL (7.05 ±1.33 mins) compared to group HR (10.13±2.53 mins). The time taken for sensory level regression by two dermatomes in group HL was 109.56 ±12.63 mins which was significantly longer than in group HR 74.80 ±7.45 mins ($p<0.01$). The total duration of analgesia was significantly longer in group HL (215.22 ±26.26 mins) when compared to group HR (148.34 ± 15.74 mins) ($p< 0.01$).

In our study onset of motor block (Bromage1) was significantly faster in group HL (3.56 ±1.13 mins) compared to group HR (7.06± 0.99 mins). In HL group, 16 (32%) patients achieved Bromage 2 and 34(68%) achieved Bromage 3 where as in HR group 22(44%) achieved Bromage 2 and 28(56%) achieved Bromage 3. The time taken to achieve Bromage 3 was significantly faster ($p<0.001$) 8.81 ± 9.00 mins in group HL compared to 12.91 ±1.48 mins in group HR. The total duration of motor block was significantly longer ($p<0.01$) in group HL (158.16 ±22.76 mins) than in group HR (95.98±14.06 mins).

Regarding haemodynamic changes there were no significant alterations in the parameters (HR, SBP, DBP and MAP) between the two groups($p>0.05$) at various time intervals. Variations in mean HR and MAP are shown in Figures 1 and 2 respectively.

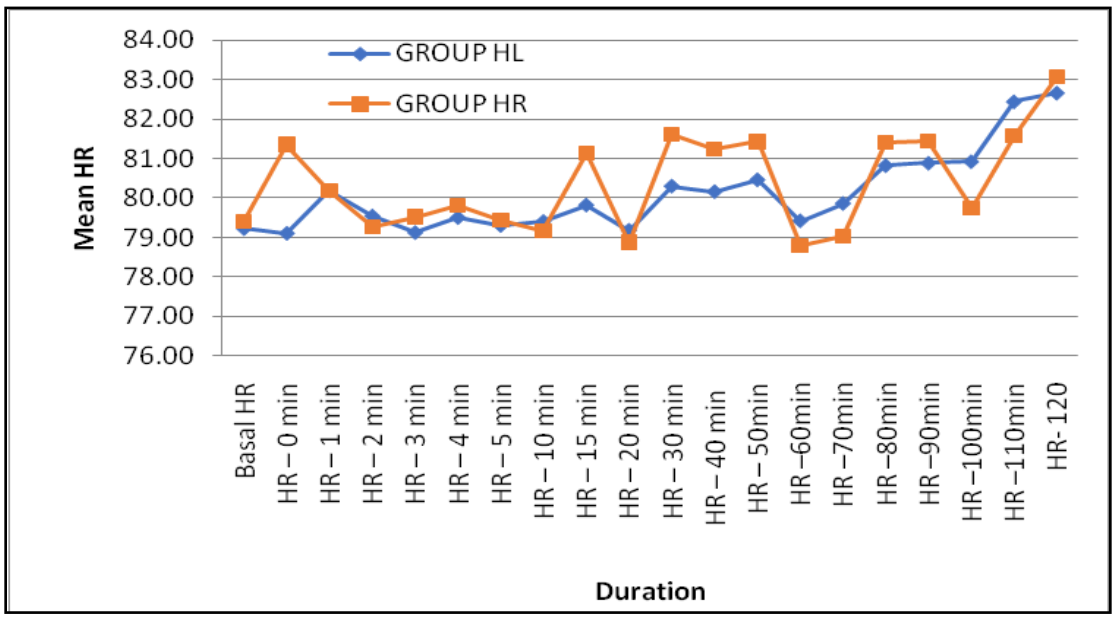

Figure 1: Showing changes in mean heart rate (in bpm) at various time intervals

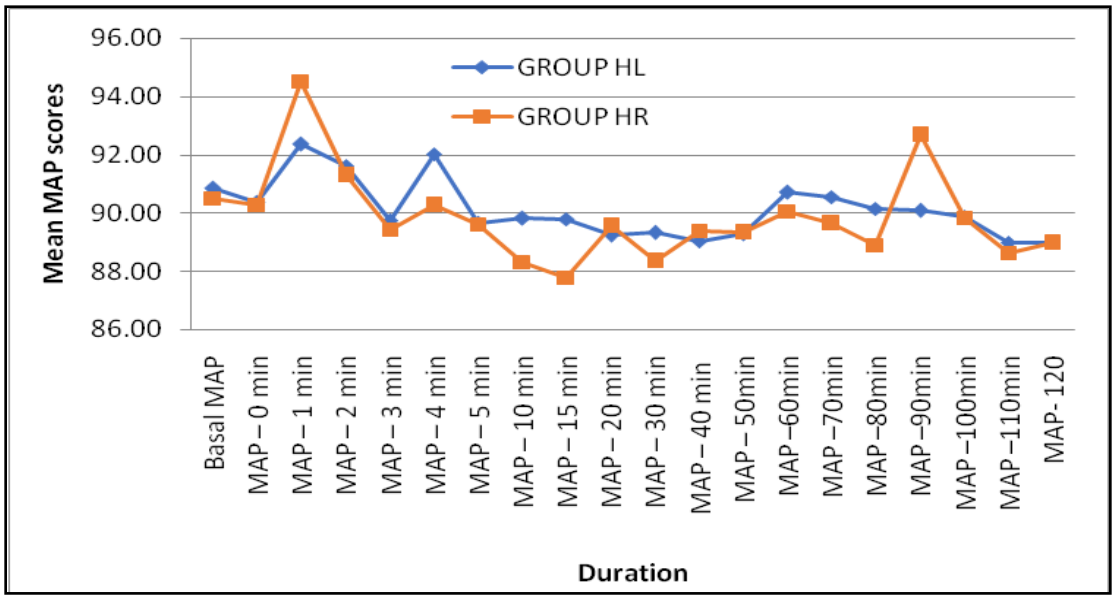

Figure 2: Showing mean arterial blood pressure changes (in mm of Hg) at various time intervals.

Table 4 shows the number of patients developing significant hypotension in group HL and group HR. There was no statistically significant difference observed between the groups with respect to side effects.

Table 4: Incidence of hypotension and bradycardia in both the groups

	Group HL	**Group HR**	**p-value**
Hypotension(n)	2 (50)	1(50)	0.701(NS)
Bradycardia(n)	2 (50)	1(50)	0.701(NS)

NS- not significant (p >0.05)

Discussion:

Bupivacaine, the most commonly used local anaesthetic for spinal anaesthesia was introduced into clinical practice in 1963 and proved to be a very effective long-acting local anaesthetic agent. In 1979, Albright drew attention to the dangers of the longer acting local anaesthetic agents, bupivacaine and etidocaine, in case they gained accidental intravascular access, resulting in cardiac arrest.[11] This led to a quest for local anaesthetic agents which are similar to bupivacaine but have minimal effects on the cardiovascular system and can be used for day-care surgeries.

Anaesthetic drugs as pure S-enantiomers, Levobupivacaine and Ropivacaine have been introduced and used since last few years due to their lower toxic effects on heart and central nervous system compared to Bupivacaine. Many clinical studies have indicated that Levobupivacaine has pharmacokinetic characteristics similar to bupivacaine[12,13] and Ropivacaine is less potent than bupivacaine as it has low lipid solubility and blocks nerve fibres involved in pain transmission to a greater degree than those involved in motor function.[8,9]

Most of the plain solutions exhibit variability in effects and are less predictable, so that block may be too low, inadequate for surgery or excessively high, causing side effects. Whereas hyperbaric solutions are more predictable, with greater spread in the direction of gravity and less interpatient variability.[12] In our country presently only isobaric preparations of levobupivacaine and ropivacaine are commercially available and manufactured hyperbaric forms of these drugs are unavailable for the reason of difficulty in maintaining the pharmacological stability of hyperbaric solutions for clinical use. It is interesting to know whether it is worth making them hyperbaric. [3,10] Hence the present study was conducted.

In our study, the mean time for onset of sensory block and the maximum level of sensory block achieved in group HL and group HR were comparable and was not statistically significant (p>0.05). Our study correlates with the studies conducted by Cappelleri G et al,[15] Luck JF et al [16] Casati A et al [17] and Ghimire R [18] et al. In contrast to our study, Sanansilp V et al [7] found that, the onset of sensory block was faster (2.8 ± 1.1mins) with 3 ml of 0.42% hyperbaric Levobupivacaine. That could be due to the volume used which was slightly higher (3ml) when compared to our study(2.5ml).

Time taken to achieve highest level of sensory block was faster with hyperbaric Levobupivacaine when compared to hyperbaric Ropivacaine and this difference was statistically significant (p<0.001). Our study is comparable with studies done by Cappelleri G et al [15] and Casati A et al. [17] In contrast to our study, Luck JF et al [16] found no statistically significant difference with regards to time taken to achieve highest level of sensory analgesia which was probably due to the less concentration of dextrose used (30mg/ml) by them.

In our study time for two segment sensory regression is 109.56±12.63min in HL group and 74.80±7.45 min in HR group. The difference in the mean time between the two groups was statistically significant (p<0.001). Our study correlates with study done by Sanansilp V et al [7] who also found similar result with hyperbaric Levobupivacaine (110.8±42.9 mins).

Total duration of sensory block and time taken for sensory regression to S1 in hyperbaric Levobupivacaine group were significantly prolonged when compared to hyperbaric Ropivacaine group (p < 0.001). Our study correlates with studies done by Luck JF et al,[16] Casati A et al,[17] and Cappelleri G et al. [15]

In a study by Camorcia et al,[19] the potencies for motor block of intrathecal Ropivacaine, Levobupivacaine, and Bupivacaine were compared, and weaker motor block potency and shorter duration of motor block were reported with ropivacaine group.[20] The onset of motor blockade in our study was significantly faster in hyperbaric Levobupivacaine compared to hyperbaric Ropivacaine group (p<0.001) which correlates with the study conducted by Sen H et al [21] (3mins) and Sanansilp V et al. [7]

Complete motor blockade of Bromage 3 was achieved in 34 patients in group HL and 28 patients in group HR (p=0.216). Quality of motor blockade was comparable between the two groups (p=0.216). This is consistent with the study by Luck JF et al. [16] Time taken to achieve maximum motor blockade was significantly shorter in HL group compared to HR group (p= 0.002) which correlates with the studies done by Luck JF et al,[16] Sen H et al,[21] Sanansilp V et al [7] and Kulkarni KR[10] et al. The total duration of motor block was significantly prolonged in HL group when compared to HR group (p=0.001). Our findings correlate with the studies done by Luck JF et al[16] and Casati A et al. [17]

Lipid solubility is an important determinant of local anaesthetic activity. The onset time of conduction block is directly correlated with the lipid solubility of local anaesthetic. The lesser lipid solubility of Ropivacaine may cause this drug to penetrate the large myelinated A fibers more slowly than the more lipid soluble Levobupivacaine. It is also postulated that because Ropivacaine is less lipophilic it has a greater effect on the nonmyelinated pain fibers rather than the myelinated motor fibers.[11]

No clinically significant changes were observed in haemodynamic parameters (heart rate, mean blood pressure, peripheral oxygen saturation) throughout our study. This may be related to usage of low doses of local anaesthetics. Our study correlates with the studies done by Casati A et al,[17] Luck JF et al [16] and Cappelleri G et al.[15]

Conclusion:

Both hyperbaric Levobupivacaine(10.5mg) and hyperbaric Ropivacaine (10.5mg) produce reliable and adequate spinal blockade for infraumbilical surgeries without significant haemodynamic changes. However intrathecal hyperbaric Levobupivacaine produces prolonged sensory and motor blockade compared to hyperbaric Ropivacaine. Shorter recovery profile of hyperbaric Ropivacaine makes it a useful alternative for intermediate duration surgeries.

References:

1. Attri JP, Kaur G, Kaur S, Kaur R, Mohan B, Kashyap K. Comparison of Levobupivacaine and Levobupivacaine with fentanyl in infraumbilical surgeries under spinal anaesthesia. Anesth Essays Res 2015; 9(2):178-84.
2. Horlocker TT, Wedel DJ. Density, specific gravity, and baricity of spinal anesthetic solutions at body temperature. Anesth Analg 1993;76(5):1015-8.
3. Chattopadhyay A, Maitra S, Sen S, Bhattacharjee S, Layek A, Pal S et al. Study to Compare the Analgesic Efficacy of Intrathecal Bupivacaine alone with Intrathecal Bupivacaine Midazolam Combination in Patients undergoing Elective Infraumbilical Surgery. Anesthesiology Research and Practice. 2013; Vol.2013, Article ID 567134: doi 10.1155/2013/567134.
4. Bajwa SJS, Kaur J. Clinical profile of Levobupivacaine in regional anesthesia: A systematic review. J Anaesthesiol Clin Pharmacol 2013; 29:530-9.
5. Glaser C, Marhofer P, Zimpfer G, Heinz MT, Sitzwohl C, Kapral S, et al. Levobupivacaine versus racemic Bupivacaine for spinal anesthesia. Anesth Analg 2002; 94:194-8.
6. Onur O, Sibel AM, Mustafa AK, Mehmet YA. Comparison of the effects of intrathecal different dosage of Levobupivacaine in elective day-case Arthroscopy of the knee. Middle East J Anesthesiol 2010;20(5):703-8.
7. Sanansilp V, Trivate T, Chompubai P, Visalyaputra S, Suksopee P, Permpolprasert L,et al.Clinical characteristics of spinal Levobupivacaine: hyperbaric compared with isobaric solution. Scientific World Journal 2012: doi 10.1100/2012/169076.
8. Chatterjee S, Bisui B, Mandal A, Sheet J, Sengupta S, Majumdar S, et al. Effects of intrathecal hyperbaric Ropivacaine versus hyperbaric Bupivacaine for lower limb orthopedic surgery. Anesth Essays Res 2014;8(3):349-53.
9. McNamee DA, McClelland AM, Scott S, Milligan KR, Westman L, Gustafsson U.Spinal anaesthesia: comparison of plain Ropivacaine 5 mg/ml with Bupivacaine 5 mg/ml for major orthopaedic surgery. Br J Anaesth 2002;89(5):702-6.
10. Kulkarni KR, Deshpande S, Namazi I, Singh SK, Kondilya K. A comparative evaluation of hyperbaric Ropivacaine versus hyperbaric Bupivacaine for elective surgery under spinal anesthesia. J Anaesthesiol Clin Pharmacol 2014;30(2):238.
11. Dar FA, Mushtaq MB, Khan UM. Hyperbaric spinal ropivacaine in lower limb and hip surgery: A comparison with hyperbaric Bupivacaine. J Anaesthesiol Clin Pharmacol 2015;31(4):466-70.

12. Gozaydin O, Gulen G, Atalan G, Kaydul M. Comparison of Hyperbaric Levobupivacaine with Hyperbaric Bupivacaine in Unilateral Inguinal Hernia Operations Performed Under Spinal Anesthesia. Arch Clin Exp Surg 2014; 3:1-9.
13. Singh G, Rathod NM, Patel K. Comparison of Equipotent Doses of Hyperbaric Ropivacaine and Hyperbaric Levobupivacaine in Spinal Anaesthesia for Patients Undergoing Lower Abdominal and Lower Limb Surgeries. Indian J Anesth Analg. 2019;6(1):249-54
14. Kharat PA, Deopujari RC. A Comparison of intrathecal 0.5% hyperbaric ropivacaine with 0.5% hyperbaric bupivacaine for elective surgery: A prospective, randomized, double-blind, controlled study. International Journal of Research in Medical Sciences.2021;9(2):471-478
15. Cappelleri G, Aldegheri G, Danelli G, Marchetti C, Nuzzi M, Iannandrea G et al. Spinal Anesthesia with Hyperbaric Levobupivacaine and Ropivacaine for Outpatient Knee Arthroscopy: A Prospective, Randomized, Double-Blind Study. Anesth Analg 2005;101(1):77-82.
16. Luck JF, Fettes PDW, Wildsmith JA. Spinal anaesthesia for elective surgery. A comparison of hyperbaric solutions of racemic Bupivacaine, Levobupivacaine, and Ropivacaine. Br J Anaesth 2008;101(5):705-10.
17. Casati AA, Moizo E, Marchetti C, Vinciguerra F. A Prospective, Randomized, Double-Blind Comparison of Unilateral Spinal Anesthesia with Hyperbaric Bupivacaine, Ropivacaine, or Levobupivacaine for Inguinal Herniorrhaphy. Anesth Analg 2004;99(5):1387-92.
18. Ghimire R, Gyawali M. Effectiveness of Hyperbaric Ropivacaine over Hyperbaric Bupivacaine in Spinal Anesthesia. Europasian journal of Medical Sciences 2019; 1(1):10-15
19. Camorcia M,Capogna G, Berritta C, Columb MO. The relative potencies for motor block after intrathecal ropivacaine, levobupivacaine and bupivacaine. Anesth Analg 2007Apr ;104(4):904-907
20. Thakore S, Thakore N, Chatterji R, Chatterjee CS, Nanda S. Evaluating the efficacy of low-dose hyperbaric levobupivacaine (0.5%) versus hyperbaric bupivacaine (0.5%) along with fentanyl for subarachnoid block in patients undergoing medical termination of pregnancy and sterilization: A prospective, randomized study. Journal of Obstetric Anaesthesia and Critical Care. 2018; 8:90-5
21. Sen H, Purtuloglu T, Sizlan A, Yanarates O, Ates F, Gundu I, et al. Comparison of intrathecal hyperbaric and isobaric Levobupivacaine in urological surgery. Minerva Anesthesiol 2010; 76:24-8.