Original Research Article

Comparative study of ropivacaine (0.5%) versus levobupivacaine (0.5%) as regional anesthesia in gynecological surgeries: A tertiary care hospital based study at Eastern India

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Received: 15-01-2021 / Revised: 18-02-2021 / Accepted:29-03-2021

Abstract

Introduction: Most women experience moderate to severe pain during labor and delivery, often requiring some form of pharmacologic analgesia. The lack of proper psychological preparation combined with fear and anxiety can greatly enhance the patient's sensitivity to pain and further add to the discomfort during labor and delivery. However, skillfully conducted obstetric analgesia, in addition to relieving pain and anxiety, may benefit the mother in many other ways. The aim of this prospective, randomized, double-blind study was to compare the block induced by ropivacaine (0.5%) plain and levobupivacaine (0.5%) plain in gynecological surgeries at the recommended dose range. These concentrations have provided equivalent block after epidural analgesia. **Material and methods:** This randomized, prospective, double blind study was conducted at a tertiary care hospital in Department of Anesthesia and Obstetrics & Gynaecology, Haldia, West Bengal between Jan 2019-December 2019. Fifty patients who were posted for gynecological surgeries were enrolled and randomly divided into two groups: Group R received 3.5 ml (17.5 mg) 0.5% ropivacaine plain and Group L received 3.5 ml (17.5 mg) 0.5% levobupivacaine plain. The onset and duration of sensory and motor block and any undesirable side effects were noted. **Results:** The mean sensory block onset time in levobupivacaine group was 6.23 ± 1.13 min, while it was 7.89 ± 2.74 min in ropivacaine group. The mean sensory onset time was higher in ropivacaine as compared to levobupivacaine group (P = 0.0073). The mean duration of sensory block in levobupivacaine group was 265.87 ± 79.67 min, while it was 239.89 ± 61.18 min in ropivacaine group. The mean duration of sensory block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.2021, NS). The mean motor block onset in levobupivacaine group was 5.29 ± 2.23 min, while it was 6.78 ± 2.67 min in ropivacaine group. The mean motor onset time was higher in ropivacaine group in comparison to levobupivacaine group (P = 0.0373). The mean duration of motor block in levobupivacaine group was 248.33 ± 78.18 min, while it was 209.29 ± 53.16 min in ropivacaine group. The mean duration of motor block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.0373). **Conclusion:** The mean duration of sensory block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.2021, NS). The mean motor onset time was higher in ropivacaine group in comparison to levobupivacaine group (P = 0.0373). The mean duration of motor block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.0373).

Keywords: Regional anesthesia, ropivacaine, levobupivacaine, gynecological surgeries, sensory and motor block

Introduction

Regional anesthesia techniques have seen numerous modifications over the last two decades with the advent of many new and safer local anesthetics.Bupivacaine, the widely used local anesthetic in regional anesthesia is available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, levobupivacaine, S (−) isomer and dextrobupivacaine, R (+) isomer. Severe central nervous system (CNS) and cardiovascular adverse reactions reported in the literature after inadvertent intravascular injection or intravenous regional anesthesia have been linked to the R (+) isomer of bupivacaine. The levorotatory isomers were shown to have a safer pharmacological profile[1-3] with less cardiac and neurotoxic adverse effects [3, 4]. The decreased toxicity of levobupivacaine is attributed to its faster protein binding rate [5, 6]. Based on findings that the cardiotoxicity infrequently observed with racemic bupivacaine shows enantioselectivity, i.e. it is more pronounced with the R(+)-enantiomer, the S(-)-enantiomer (levobupivacaine) has been developed for clinical use as a long acting local anaesthetic. The majority of in vitro, in vivo and human pharmacodynamic studies of nerve block indicate that levobupivacaine has similar potency to

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bupivacaine. However, levobupivacaine had a lower risk of cardiovascular and CNS toxicity than bupivacaine in animal studies. In human volunteers, levobupivacaine had less of a negative inotropic effect and, at intravenous doses >75 mg, produced less prolongation of the QTc interval than bupivacaine [7].

Ropivacaine is a new, long-acting local anaesthetic, prepared as a single enantiomer (the S form). Ropivacaine has a pKa of 8.07, a protein binding of approximately 94%, but a lower lipid solubility than bupivacaine. Extensive animal toxicological studies have shown a lower propensity for cardiotoxicity with ropivacaine than with bupivacaine. Studies in sheep have shown that the systemic toxicity of ropivacaine is not enhanced by gestation. Studies in human male volunteers have shown that ropivacaine is associated with at least 25% less CNS and cardiovascular adverse effects than bupivacaine following use of intravenous infusions of either drug at a rate of 10 mg/min, to a maximum dose of 150 to 250 mg. With its lower toxicity, especially cardiovascular toxicity, and less intense motor blockade, ropivacaine may have advantages over bupivacaine in epidural pain relief during labour [8]. Jain S et al conducted randomized, prospective, double blind study and revealed that the onset and duration of sensory and motor block and any undesirable side effects were noted. Demographic parameters were comparable between the two groups (P >0.05). Onset of sensory and motor block was significantly faster in Group L, duration of motor and sensory block was significantly less in Group R. Patients in group R were hemodynamically stable (P = 0.032) compared to group L. Both ropivacaine and levobupivacaine have the desirable blocking property and can be used in gynecological surgeries. Ropivacaine showed shorter duration of sensory and motor block allowed early mobilization and early recovery of patients [9]. Levobupivacaine is a long acting local anesthetic with less cardiovascular toxicity. Recently we can use levobupivacaine for postoperative analgesia. We prospectively compared levobupivacaine with ropivacaine for the postoperative epidural analgesia in patients undergoing gynecological surgeries. So present study had compared newer local anesthetics in terms of clinical and anesthetic properties and to provide observations in spinal anesthesia for gynecological surgeries.

Material and methods

A prospective randomized double blind study was done in a tertiary care hospital in Department of Anesthesia and Obstetrics & Gynaecology, Haldia, West Bengal between Jan 2019-December 2019. Fifty patients who were posted for gynecological surgeries were enrolled and randomly divided into two groups: Group R received 3.5 ml (17.5 mg) 0.5% ropivacaine plain and Group L received 3.5 ml (17.5 mg) 0.5% levobupivacaine plain. The onset and duration of sensory and motor block and any undesirable side effects were noted. This study has included 50 female patients of age between 20-70 years between 50-80 kg of ASAI-II physical status, posted for elective gynecological surgeries. A written informed consent from patients and approval from Institutional Ethics Committee was obtained before starting the study. Patients who had severe bronchopulmonary disease, any coagulation disorder, any neuromuscular disease, hypersensitivity to local anesthetic, contraindication to spinal anaesthesia as infection at puncture site, spinal deformity, patients who refused were excluded from study. Patients were randomly distributed into two groups of 25 patients each and randomization was done by lottery method. Group L (n=25) received 17.5 mg plain levobupivacaine (3.5 ml), Group R (n=25) received 17.5 mg plain ropivacaine (3.5 ml). On arrival in anesthesia room a 20 gauze intravenous cannula was inserted and 15 ml/kg ringer lactate solution was infused. Monitored parameters include 3-lead ECG, heart rate (bpm), non-invasive blood pressure (NIBP, mm Hg), pulse oximetry (SpO_2%). Spinal anesthesia was obtained by 0.5% plain levobupivacaine 3.5 ml (Group L) or 0.5% plain ropivacaine 3.5 ml (Group R). Syringe of drugs was prepared by an anesthesiologist who was not part of the study further. In sitting position, either of the drugs was aseptically administered through 25G Quincks needle between L3-L4, L4-L5 interspace. As soon as the subarachnoid block was performed patients place in supine position. Sensory block was graded according to Gromley and Hill test using a pin protruding through a guard every 2 min till no sensation was achieved at T8 level. Motor block was graded according to Modified Bromage Scale (0-3), where 0=no motor block (full flexion of hip knee and ankle), 1=ability to move knees and feet, inability to flex hip, 2=ability to move feet only, inability to flex hip or knee, 3=full motor block) respectively [10, 11]. The onset time of sensory block was assessed referring to the interval between spinal puncture and the maximal pinprick score. The onset time of motor block was assessed evaluating the time interval between puncture and the maximal definitive Bromage score. The offset time was considered as corresponding return to normal sensitivity and motility. The spread of anesthesia was refer to the upper dermatome with any grade of sensory impairment. Any side effects like nausea, vomiting, pain, shivering, sedation, hypotension, bradycardia and respiratory discomfort was noted and treated with appropriate drug if required. The surgical procedure was start within 30 min of spinal puncture. The management of the patient being switched to general anesthesia in case of score less than Bromage 2 and excluded from the study. Time interval for anesthesia parameters was checked every 2 min till 30 min to note onset and maximum degree of block. Vital parameters was recorded at 0, 5, 10, 15, 20, 25, 30, 45 and 60 min and then every fifteen min till surgery ended, than every hourly postoperatively until motility and sensitivity returns back to basal condition. A decrease in heart rate more than 50 and decrease in MAP more than 20% from basal value was considered as bradycardia and hypotension and treated with Inj. Atropine 0.5 mg and Inj. Mephentermine 6 mg bolus dose repeated as needed. Every patient received supplemental oxygen through face mask with spontaneous breathing. Inj. Diclofenac in 75 mg used as rescue analgesic (if not contraindicated) the maximal dose would be three times a day. In patients where diclofenac is contraindicated, Inj. Tramadol was administered. The mean comparison between the two groups was done using unpaired 't' test, two group proportions were compared using Z test for two sample proportion. A P value of <0.05 was taken as statistically significant. Online statistical software was used for analysis of the data.

Results

The mean age in Group L was 43.92 ± 13.11 years and in Group R it was 49.18 ± 10.17 years. The mean age in both the groups was comparable (P = 0.1195, NS) [Table 1]. The mean weight in Group L was 62.13 ± 7.53 years and in Group R it was 64.11 ± 8.47 years. The mean weight in both the groups was comparable (P = 0.3867, NS) [Table 1].The mean sensory block onset time in levobupivacaine group was 6.23 ± 1.13 min, while it was 7.89 ± 2.74 min in ropivacaine group. The mean sensory onset time was higher in ropivacaine as compared to levobupivacaine group (P = 0.0073). The mean duration of sensory block in levobupivacaine group was 265.87 ± 79.67 min, while it was 239.89 ± 61.18 min in ropivacaine group. The mean duration of sensory block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.2021, NS). The mean motor block onset in levobupivacaine group was 5.29 ± 2.23 min, while it was 6.78 ± 2.67 min in ropivacaine group. The mean motor onset time was higher in ropivacaine group in comparison to levobupivacaine group (P = 0.0373). The mean duration of motor block in levobupivacaine group was 248.33 ± 78.18 min, while it was 209.29 ± 53.16 min in ropivacaine group. The mean duration of motor block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.0373) [Table 1].

Table 1: Comparison of various parameters between ropivacaine and levobupivacaine groups (n=50)

Parameter	Levobupivacaine [Mean±SD]	Ropivacaine[Mean±SD]	't' Value	P Value
Age (years)	43.92 ± 13.11	49.18 ± 10.17	1.585, df=48	P = 0.1195, NS
Weight (kg)	62.13 ± 7.53	64.11 ± 8.47	0.874, df=48	P = 0.3867, NS
Sensory block onset (min)	6.23 ± 1.13	7.89 ± 2.74	2.800, df=48	P = 0.0073*
Duration of sensory block (min)	265.87 ± 79.67	239.89 ± 61.18	-1.293, df=48	P = 0.2021, NS
Motor block onset (min)	5.29 ± 2.23	6.78 ± 2.67	2.142, df=48	P = 0.0373*
Duration of motor block (min)	248.33 ± 78.18	209.29 ± 53.16	-2.065, df=48	P = 0.0444*

Unpaired 't' test applied. P value < 0.05 was taken as statistically significant

Bradycardia (12%) was higher in levobupivacaine group in comparison to 4% in ropivacaine group. Bradycardia was comparable between both the groups (P=0.0151), while incidence of hypotension was higher in levobupivacaine group (20%) in comparison to the ropivacaine group (4%) (P = 0.0848) [Table 2].

Table 2: Comparison of complications between ropivacaine and levobupivacaine groups (n=50)

Complications	Levobupivacaine Group(n=25)		Ropivacaine Group(n=25)		Z value	P Value
	No.	%	No.	%		
Bradycardia	3	12	1	4	2.4254	P=0.0151*, p < 0.05
Hypotension	5	20	1	4	4.5291	P = 0.0848, NS
Total	25	100.0	25	100.0		

****Z test for two sample proportion applied. P value < 0.05 was taken as statistically significant***

Discussion

Epidural analgesia is well established as a means of providing pain relief during labour. However, in achieving this there may be a price to pay in terms of motor block during labour and expulsive effort in the second stage. Preservation of muscle power is important as it enables the labouring woman to be mobile in bed, maintains a greater sense of control and reduces her dependency on attending midwifery staff. Strategies to reduce motor blockade include using lower concentrations of local anaesthetics with the addition of opioids [12], or by using newer local anaesthetic agents, e.g. ropivacaine [11, 13]. The degree of motor block associated with epidural analgesia has classically been assessed using the modified Bromage Score [14].

Grade 0 No motor block

Grade 1 Inability to raise extended leg, able to move knees and feet

Grade 2 Inability to raise extended leg and move knee, able to move feet

Grade 3 Complete motor block of the lower limbs.

González-Suárez S et study revealed that onset of motor block was 9.0 mins (SD, 5.3 mins) for ropivacaine and 12.4 mins (SD, 7.8 mins) for levobupivacaine (P = 0.02). Time to be considered ready for surgery was similar in both groups: ropivacaine, 25.2 mins (SD, 5.1 mins); and levobupivacaine, 25.3 mins (SD, 6.4 mins) (t = −0.09, P = 0.93). Sensory block was 9.2 hrs (SD, 3.1 hrs) for ropivacaine and 11.3 hrs (SD, 4.1 hrs) for levobupivacaine **(**P = 0.01). Onset of motor block was significantly faster for ropivacaine than levobupivacaine (P = 0.02), but the time to be ready for surgery was similar with both drugs. Duration of sensory block was prolonged with levobupivacaine (P = 0.01) [15]. Randomised, double-blind clinical studies established that the anaesthetic and/or analgesic effects of levobupivacaine were largely similar to those of bupivacaine at the same dose. Sensory block tended to be longer with levobupivacaine than bupivacaine, amounting to a difference of 23 to 45 minutes with epidural administration and approximately 2 hours with peripheral nerve block. With epidural administration, levobupivacaine produced less prolonged motor block than sensory block. This differential was not seen with peripheral nerve block. Conditions satisfactory for surgery and good pain management were achieved by use of local infiltration or peribulbar administration of levobupivacaine. Levobupivacaine was generally as effective as bupivacaine for pain management during labour, and was effective for the management of postoperative pain, especially when combined with clonidine, morphine or fentanyl [16]. Wang Y et al study revealed that there were significant differences in T0, T2, T3, and Bromage score between the 2 groups (p < 0.05), while there were no remarkable differences in T1 and the total amount of dosage (p > 0.05). Levobupivacaine has excellent anesthetic effect in epidural anesthesia for gynecology and it is suitable for clinical use [17].

Lee YY et al study revealed that the ED(50)s were 5.50 mg for bupivacaine (95% confidence interval [CI]: 4.90-6.10 mg), 5.68 mg for levobupivacaine (95% CI: 4.92-6.44 mg), and 8.41 mg for ropivacaine (95% CI: 7.15-9.67 mg) in intrathecal anesthesia. The relative anesthetic potency ratios are 0.97 (95% CI: 0.81-1.17) for levobupivacaine/bupivacaine,0.65(95%CI:0.54-0.80) for ropivacaine/ bupivacaine,and 0.68(95%CI:0.55-0.84) for ropivacaine/ levobupivacaine. Study suggests that in intrathecal anesthesia for lower limb surgery, ropivacaine is less potent than levobupivacaine and bupivacaine, whereas the potency is similar between levobupivacaine and bupivacaine [18].

Analgesia duration was significantly longer in ROPI-SUF and LBUPI-SUF than in BUPI-SUF administered women with a mean difference (95% CI) of 16.12 (2.56, 29.68); P < 0.03 and 18.02 (9.09, 26.96); P < 0.0001 respectively under a random effects model (REM). Effective analgesia achievement was significantly earlier in the BUPI-SUF than in either the ROPI-SUF (2.61 [1.87, 3.36]; P < 0.00001) or the LBUPI-SUF groups (4.53 [3.66, 5.40]; P < 0.00001) under a fixed effects model (FEM) but not under a REM (I(2)= 85%). Motor blockade incidence was higher in BUPI-SUF anesthetized patients, although the difference was not statistically significant. Whereas significantly longer labor analgesia can be achieved with ROPI-SUF and LBUPI-SUF and ropivacaine is associated with comparatively less motor blockade, labor duration after epidural analgesia has been found to be shorter in BUPI-SUF and there is a low incidence of instrumental delivery [19]. Goyagi T et al study revealed that there was no difference in demographic data between the levobupivacaine and ropivacaine groups. In the levobupivacaine group (n=23) the patient received epidural 0.24% levobupivacaine and fentanyl, while the patients in the ropivacaine group (n=43) epidural 0.19% ropivacaine and fentanyl, at the rate of 3.5 ml x hr(-1). The volume of epidural fentanyl was similar between the groups. The time from the end of surgery to receive the first analgesic was longer in the levobupivacaine group than in the ropivacaine group. The number of the patients who did not require additional analgesia was greater in the levobupivacaine group than in the ropivacaine group. The patients who received metocropramide to

treat nausea were fewer in the levobupivacaine group, compared with the ropivacaine group. These results suggest that the use of epidural 0.24% levobupivacaine in the patients undergoing the gynecological surgery is superior to the use of 0.19% ropivacaine [20].

Pathak N et al study revealed that the differences in VAS Score of subjects of both the groups were statistically significant($p<0.05$) at 18 hrs, 24hrs, 36hrs and 48 hrs and the differences in Modified Bromage Scale of subjects of the groups were statistically similar at most of the time intervals. Also, the side effects were statistically similar between the groups. Authors concluded that ropivacaine-fentanyl is better than ropivacaine alone by continuous epidural infusion for post-operative analgesia in major gynecological surgeries with no statistically significant side effects, effect on ambulation being similar in both the groups [21].

Altienzar MC et al conducted a randomised study for patients in labour and found that 0.1% ropivacaine with fentanyl 2 microg/ mL via epidural was adequate for analgesia in first stage of labour[20]. The quality of pain relief was similar to that obtained using 0.2% ropivacaine with fentanyl 2microg/mL and there was no difference in motor or sensory block [22].

The limitations of our study are small sample size, lack of continuous monitoring of hemodynamic parameters and that it was limited to female population and we could not assess the effect of drugs on male population.

Conclusion

Both ropivacaine and bupivacaine having the desirable blocking property of racemic bupivacaine can be used for gynecological surgeries.The mean duration of sensory block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.2021, NS). The mean motor onset time was higher in ropivacaine group in comparison to levobupivacaine group (P = 0.0373). The mean duration of motor block was higher in levobupivacaine group in comparison to ropivacaine group (P = 0.0373).

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Conflict of Interest: Nil Source of support:Nil