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Randomized controlled study comparing a isobaric levobupivacaine to a conventional dose of hyperbaric bupivacaine for infra umbilical surgeries

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***Abstract*---**Levobupivacaine is an attractive alternative to racemic bupivacaine for spinal anesthesia due to the lower potential for cardio-toxicity and faster recovery profile. Present study is undertaken to compare hemodynamic and analgesic characteristics using an isobaric levobupivacaine to a conventional dose of hyperbaric bupivacaine for infra umbilical surgeries. A prospective randomized double blind study was conducted involving 60 patients belonging to ASA gr I & II coming for elective lower abdominal surgeries. They were randomly divided into 2 groups of 30 each. Group I received 3ml of 0.5% hyperbaric bupivacaine, group II received 3ml of 0.5% isobaric levobupivacaine. Hemodynamic parameters like heart rate, NIBP and SpO2 were monitored every 15mins till end of surgery and for 2 hours post operatively. Incidence of side effects such as hypotension, bradycardia and nausea and vomiting were noted. Demographic parameters in both groups were comparable. Onset of sensory block was slow in group L. Level of sensory block was comparable and duration of analgesia at L1 (L1regression) was significantly shorter with Levobupivacaine compared to Bupivacaine.

Onset of motor blockade was slower and duration of motor blockade was also shorter with levobupivacaine compared to bupivacaine. However all the patients in either group attained complete motor blockade. With respect to hemodynamic parameters intrathecal Levobupivacaine provided a higher degree of cardiovascular stability with a lesser incidence of hypotension and bradycardia. There was no incidence of side effects like Nausea, vomiting, Shivering or PDPH in either group. Bupivacaine, with same level of maximum sensory block, duration of analgesia at L4 (L4 regression) was significantly same with Levobupivacaine. Cardiovascular stability is better than Bupivacaine. Hence Levobupivacaine can be used successfully for lower abdominal surgeries where early.

***Keywords*---**bupivacaine, levobupivacaine, cardiovascular stability, abdominal surgeries.

Introduction

Subarachnoid block is the anaesthesia technique of choice and is gold standard for lower abdominal /lower limb surgery compared to general and epidural anesthesia, as there is chance of aspiration syndrome with the former and lack of reliability of block with epidural anesthesia. Hence a study will be conducted to study and compare the efficacy and safety of Subarachnoid anaesthesia (SAB) is the most popular as well as effective technique for infraumbilical surgeries. Currently, 0.5% hyperbaric Bupivacaine hydrochloride is extensively used because of its longer duration of motor and sensory blockade. But it carries an increased risk of cardiac and central nervous system toxicity, if an inadvertent intravenous injection occurs.[1,2]

Levobupivacaine is an amide type local anaesthetic that is S-enantiomer of racemic bupivacaine with 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. Reports using levobupivacaine for epidural or brachial plexus anaesthesia suggested equivalent clinical efficacy to bupivacaine. However, inadequate data for its use in spinal anaesthesia are available. intrathecal isobaric Hence a study will be conducted to study and compare the efficacy and safety of intrathecal isobaric Levobupivacaine with hyperbaric Bupivacaine.

Materials and Methods

It is a prospective randomized double blind study was conducted on 60 patients undergoing elective lower abdominal/limb surgery under subarachnoid block at Gandhi hospital, secunderabad,Telangana state during June 2012 to October 2014.

Inclusion Criteria

Patients aged between 18 years and 55 years height more than 150 cm under ASA grade I and II, undergoing elective surgeries.

Exclusion Criteria

Patients having deformities of spine and infection at the site of insertion of spinal needle, bleeding disorders/ coagulation abnormalities/raised intra cranial pressure**,** posted for emergency surgeries, having neurological deficit, who fail to achieve desired sensory and motor blockade with history of severe migraine and headache due to other causes.

Preanesthetic Examination and Preparation

The study protocol was approved by Hospital Ethics committee and Ethical clearance was obtained from the institution for the study. Preanesthetic checkup was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations recorded. The procedure of spinal anesthesia was explained to the patients and written informed consent was obtained. Patients advised overnight fasting and premedicated with Tab.Ranitidine150mg, and Tab.Alprazolam 0.5mg. Patient was preloaded with an i.v.infusion of one liter of Ringer lactate solution.

Method

Sixty patients were randomly divided into two groups of thirty each.

- Group B: Thirty patients received 3miof injection 0.5% hyperbaric Bupivacaine intrathecally.
- Group L: Thirty patients received 3mi of 0.5% levobupivacaine intrathecally.

Preparation of Boyle's anesthesia machine was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet and working suction apparatus were kept ready before the procedure. After shifting the patient to operating theatre, IV access was obtained on the forearm with 18 Gauge IV cannula and IV infusion started with Ringer Lactate. Patients were monitored for heart rate (HR), noninvasive blood pressure (NIBP), percentage oxygen saturation (SpO_2). Under all aseptic precautions spinal anesthesia was performed with the patient in the lateral position using a 25-gauge Quincke needle at the L3-4 interspaces. The study solution (3ml) was administered over 30sec. Patient was turned gently and placed supine without elevation of extremities and tested every 5 minutes until maximal spread of sensory blockade, then every 15 minutes during the operation.

Patients were considered hypotensive when their mean arterial pressure decreased to less than 25% from baseline and were treated with injection Ephedrine 6 mg intravenously, dose titrated according to response. A decrease in the heart rate to less than 60 beats per minute was treated with injection atropine 0.02 mg/kg intravenously. Highest level of sensory block, Onset time

for highest level of sensory block, Maximal level of motor block, Onset time for maximal motor block, Onset and offset time for motor blockade, Duration of both sensory and motor block was recorded during intraoperative period. Complications such as nausea, vomiting and shivering as well as the treatment given were noted down. At the end of surgery the quality of analgesia was judged according to patient's description, as follows:

- Excellent - No discomfort or pain
- Good - Mild pain / discomfort, no need for additional analgesics.
- Poor - Moderate to severe pain that required additional analgesics.

All the patients were observed during the post-operative period for 2 hours and later 6th hourly to know the duration, quality and intensity of pain. The patients were also observed for the development of PDPH and were followed up for 3-4days.

Statistical Methods

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean+/- SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, Assumptions:

- Dependent variables should be normally distributed,
- Samples drawn

From the population should be random, Cases of the samples should be independent. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Inter group analysis) on metric parameters. Leven1s test for homogeneity of variance has been performed to assess the homogeneity of variance. Mann Whitney U test has been used to find the significance between two groups for parameters on non-interval scale. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Mean Unknown population size

$$n = (z^2 * ı^2) / ME^2$$

Results

Table1
Demographic distribution of patients studied

Age in years	Group B		Group L	
	No	%	No	%
20-30	9	30.0	6	20.0
31-40	2	6.7	8	26.7
41-50	14	46.7	11	36.7

51-60	5	16.7	5	16.7
Total	30	100.0	30	100.0
Mean ± SD	41.97±12.29		41.97±11.11	
Gender				
Male	21	70.0	21	70.0
Female	9	30.0	9	30.0
Height (cm)	164.57±5.22		164.03±5.22	
Weight (kg)	54.53±7.48		55.23±8.81	
BMI (kg/m^2)	20.05±1.98		20.41±2.49	

Table 2
Type of surgery done in patients studied

Type of surgery	Number of patients	%
TURP	7	11.7
Mesh repair	5	8.3
ORIF with DHS	4	6.7
Trendelenburg Procedure	4	6.7
Excision	3	5.0
Lithotripsy	3	5.0
Lithotripsy+Stenting	3	5.0
Mesh Repair	3	5.0
ORIF with IM nailing	3	5.0
Below Knee amputation	2	3.3
CRIF with I.M nailing	2	3.3
Debridement+Disarticulation	2	3.3
Meatoplasty	2	3.3
ORIF with Bone Graft	2	3.3
ORIF with Plate and screws	3	5.0
ORIF with TBW	2	3.3
SSG	2	3.3
Ureteroscopy+Lithotripsy	2	3.3
AMP	1	1.7
Hemorrhoidectomy	1	1.7
Jaboulays Procedure	1	1.7
Lateral Sphincterotomy	1	1.7
LT High Inguinal Orchidectomy	1	1.7
ORIF with K Wires and Screws	1	1.7

Table 3
Comparison of Onset and duration time for sensory and motor block (Seconds) in two groups of patients

Onset time for sensory block	Group B	Group L
Min-Max	20-40	156-180
Mean ± SD	31.17±6.11	168.90±7.61
Inference	Onset time for sensory block is significantly more Group L with P<0.001**	
Maximum level of sensory block		
T10	0	0
T8	30(100.0%)	30(100.0%)
T6	0	0
Duration of maximum sensory	182.67±20.29	190.33±9.37
Inference	Onset time for sensory block is significantly more Group L with P<0.05*	
Duration of motor block	218.50±19.17	149.00±3.81
Inference	Onset time for sensory block is significantly more Group L with P<0.001**	

Duration of motor block was less in group L compared to group B and this is both clinically and statistically significant.

Table 4
Comparison median modified bromage score in two groups of patients

Modified Bromage score	Group B	Group L	P value
5 minutes	3.00	2.00	<0.001**
10 minutes	3.00	2.00	<0.001**
15 minutes	3.00	3.00	1.000
30 minutes	3.00	3.00	1.000
45 minutes	3.00	3.00	1.000
60 minutes	3.00	3.00	1.000
90 minutes	3.00	3.00	1.000
120 minutes	3.00	3.00	1.000

Mann Whitney U test. Median time for onset of motor block was longer in group L and this is clinically and statistically significant.

Table 5
Duration of post-operative spinal level in two groups of patients

Spinal level	Group B	Group L	P value
T10	206.00±34.28	310.33±9.37	0.031*

T12	208.67±19.07	209.00±10.37	0.933
L4	232.00±16.59	224.00±10.37	0.029*

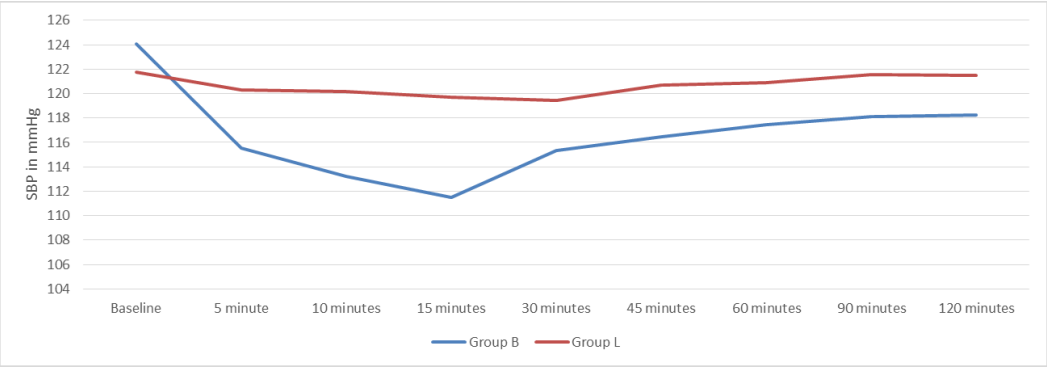

Figure 1. Comparison of SBP (mm Hg) in two groups of patients

Fall in Systolic blood pressure was observed in both the groups following institution of spinal anaesthesia. The maximum fall was observed during 5th min to 45th min in group B and 15th min to 30th min in group L. The magnitude of fall varied between 8mm Hg to 40mm Hg in group B and 1mm Hg to 20mm Hg in group L. This was clinically and statistically significant.

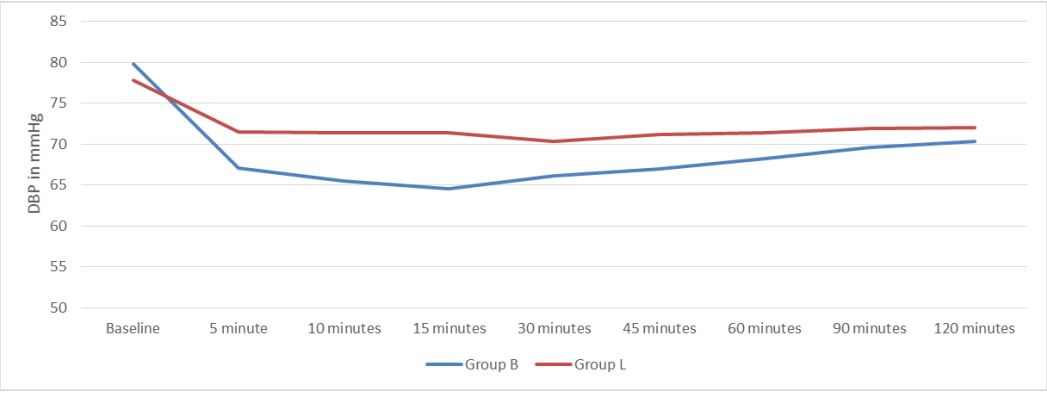

Figure 2. Comparison f DBP (mm Hg) in two groups of patients

There was fall in diastolic blood pressure following spinal anaesthesia in group B. The fall was observed between 5th min to 45th min. The magnitude of fall ranged from 10mm Hg to 20mm Hg. There was no significant fall in diastolic blood pressure in group L. This is both clinically and statistically significant. In concurrence with fall in systolic and diastolic blood pressure, there was fall in mean arterial pressure also following subarachnoid block. The median fall was 15mm Hg in group B and 6mm Hg in group

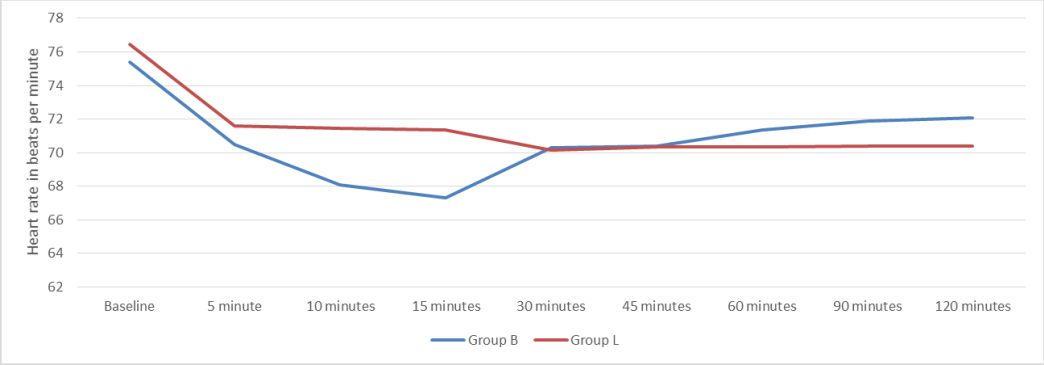

Figure 3. Comparison of Heart rate (bpm) in two groups of patients

There was no significant change in heart rate following subarachnoid block in group L. The median fall in heart rate in group B was 7 beats and this was observed between 5th min to 15th min following spinal anaesthesia.

Table 6
Comparison of complications in two groups

Complications	Group B (n=30)	Group L (n=30)
Nil	19(63.3%)	30(100.0%)
Yes	11(36.7%)	0
Bradycardia(B)	7(23.3%)	0
Hypotension(H)	3(10.0%)	0
B/H	1(3.3%)	0
Inference	Incidence of complications are significantly more in Group B with P<0.001**	

+ Suggestive significance (P value: 0.05<P<0.10) <
* Moderately significant (P value 0.05)
** Strongly significant (P value: P<0.01)

Discussion

Subarachnoid block is a commonly employed anesthetic technique for performing lower abdominal surgeries. It is a safe, inexpensive and easy-to-administer technique which also offers a high level of post-anesthesia satisfaction for patients. The technique is simple, has rapid onset and is reliable. The risk of general anesthesia, including mishaps due to airway management, aspiration and polypharmacy are avoided by this technique. Bupivacaine is the local anesthetic used routinely for lower limb/abdominal surgeries because of its high potency and minimal neurological symptoms. Though cardiotoxicity is not a concern in subarachnoid block, the quality of sensory blockade, motor blockade, hemodynamic changes and side effect profile are some considerations in selecting a drug for spinal anesthesia. Levobupivacaine, a s-enantiomer[28] of bupivacaine is being increasingly used for spinal anesthesia in caesarean section, lower abdominal and perineal surgeries

including lower limb surgeries. Advantages claimed are shorter duration of motor block with similar sensory block properties compared to bupivacaine. Thus it minimizes the psychological discomfort of being immobile for long time. Also its major advantage is lesser cardiotoxic property compared to bupivacaine hence this study was conducted to assess the sensory and motor characteristics of levobupivacaine for spinal anesthesia in lower limb/abdominal surgeries.

A prospective, randomized controlled double blind study was done at Gandhi hospital secunderabad involving 60 ASA I and II parturients who underwent lower abdominal surgeries under sub arachnoids block. In our study we have used a ratio of 1:1 by volume in order to know the minimum possible dosage of both the drugs to obtain adequate Anaesthesia. Isobaric levobupivacaine 15mg and Hyperbaric Bupivacaine 15mg was used. In our study 3 patients in group B required treatment for intra-operative hypotension, 7 patients required treatment for bradycardia and 1 patient required treatment for both hypotension and bradycardia but there was no incidence of intraoperative hypotension or bradycardia requiring treatment in group L.

Christian Glaser, Peter Marhofer et al[3] evaluated the anaesthetic potencies and hemodynamics of intrathecal isobaric levobupivacaine compared with isobaric bupivacaine in eighty ASA I-III patients undergoing total hip replacement and they concluded that both show equally effective potencies for spinal anesthesia, both with regard to the onset time and the duration of sensory and motor blockade. Intrathecal administration resulted in similar hemodynamic changes regardless of whether levobupivacaine or racemic bupivacaine was used. Hence their conclusion was that levobupivacaine seems to be an interesting alternative to bupivacaine for spinal anesthesia. J.F. Luck , P.D.W. Fettes and J.A.W. Wildsmith[4] in their study in eighty patients undergoing elective infraumbilical surgeries comparing clinical effects of hyperbaric bupivacaine for spinal anaesthesia with similar preparations of levobupivacaine and ropivacaine. They found out that bupivacaine and levobupivacaine were clinically indistinguishable and ropivacaine provided reliable spinal anaesthesia with shorter duration than bupivacaine or levobupivacaine.

Alley et al [5]conducted a randomized, double blind, cross-over study in healthy volunteers in 2002 to compare 0.25% hyperbaric levobupivacaine and racemic bupivacaine for spinal anaesthesia. They concluded that hyperbaric spinal levobupivacaine has equivalent clinical efficacy to hyperbaric bupivacaine for spinal anaesthesia in doses from 4 to12 mg. The frequency of adverse events was also similar with both the drugs. They determined that the relative clinical efficacy of bupivacaine to levobupivacaine in spinal anesthesia is approximately 1:1. Equal milligram doses of spinal levobupivacaine provide a similar profile to bupivacaine for sensory and motor block as well as time until achievement of discharge criteria and hence concluded that levobupivacaine is an alternative to bupivacaine without offering any specific clinical advantage when used in spinal anaesthesia

Coppejans H C, Vercauteren[6] in their study compared effects of spinal levobupivacaine with bupivacaine for caesarean section. They used bupivacaine

6.6 mg, levobupivacaine 6.6mg or ropivacaine 10 mg, all in combination with sufentanil 3.3 µg. They found lower incidence of hypotension with the S-enantiomer levobupivacaine. There was no statistical difference in requirement of additional analgesics and vasopressor use between both groups. Finally concluded that spinal levobupivacaine for cesarean section causes less hypotension and motor block than racemic bupivacaine. (7)

Casati and co workers[7] publish that was conducted in 60 patients undergoing inguinal hernia repair and compared the clinical profile of unilateral spinal anesthesia produced with either 8 mg of hyperbaric bupivacaine 0.5% (*n*=20), 8mg of hyperbaric levobupivacaine 0.5% (*n*=20), or 12 mg of hyperbaric ropivacaine 0.5% (*n* =20). They hence demonstrate that 8 mg of levobupivacaine or 12 mg of ropivacaine are acceptable alternatives to 8 mg of bupivacaine when limiting spinal anesthesia at the operative side for inguinal hernia repair. Interestingly, the use of a 1.5 to 1 equipotency ratio between ropivacaine and levobupivacaine or bupivacaine resulted, nevertheless, in a shorter duration of spinal anesthesia, even if this was not associated with a shorter home discharge time.

OpasVanna et al [8]conducted a study in 2006 to investigate the clinical efficacy and safety of isobaric levobupivacaine compared with hyperbaric solution of Bupivacaine in spinal anaesthesia for transurethral endoscopic surgery and concluded that 2.5 ml of 0.5% isobaric levobupivacaine and 0.5% hyperbaric bupivacaine show equally effective potencies with regard to both onset time and duration of sensory blockade. Levobupivacaine generally showed a more sustained sensory and motor blockade. Intrathecal administration resulted in similar hemodynamic changes and adverse events regardless of whether isobaric levobupivacaine or hyperbaric of racemic bupivacaine was used. Lee YY et al.[9] conducted a prospective, randomized, double-blind trial of 75 patients to compare the potencies of Levobupivacaine, Ropivacaine, and Bupivacaine when given intrathecally using a combined spinal-epidural technique in patients having lower limb surgery lasting for a duration of up to 50 min. They suggested that for intrathecal anaesthesia for lower limb surgery, Ropivacaine is less potent than Levobupivacaine and Bupivacaine, whereas the potency is similar between Levobupivacaine and Bupivacaine.

Frawly G and colleagues[10] did a study in comparing the relative potency of new local anaesthetics such as levobupivacaine and ropivacaine with bupivacaine by the minimum local analgesic concentration model for neonatal spinal anaesthesia in patients who had elective lower extremity and hip operations. They concluded that the appropriate doses for infant spinal anaesthesia are 1 mg kg (-1) of isobaric 0.5% bupivacaine and ropivacaine and 1.2 mg kg(-1) of isobaric 0.5% levobupivacaine. The relative potency ratios at the ED (50) were bupivacaine: levobupivacaine 0.55 (95% CI 0.39-0.88), bupivacaine: ropivacaine 0.61 (0.41-1.00), and levobupivacaine: ropivacaine 1.09 (0.84-1.45). A study was conducted by Hakan E R and his colleagues[11] on sixty patients undergoing transurethral procedures under subarachnoid block with either 7.5 mg hyperbaric bupivacaine plus 25 µg fentanyl or 7.5 mg hyperbaric levobupivacaine plus 25 µg fentanyl intrathecally. They concluded that both techniques provide adequate spinal block and have few similar side effects for

transurethral surgery, the use of low-dose hyperbaric levobupivacaine plus fentanyl may be preferable to low-dose hyperbaric bupivacaine plus fentanyl because of the reduced motor block, shorter duration of motor block, longer duration of sensory block and longer time to the first requirement for analgesia.

Kazak et al [12]conducted a study with the aim to compare the reliability, suitability and the side effects of the spinal blocks produced by hyperbaric solutions of levobupivacaine, ropivacaine and bupivacaine in patients undergoing total hip or knee arthroplasty. Patients were randomized into three groups: the first group received 15 mg of 0.5% hyperbaric bupivacaine (group HB, n=30), the second group received 15 mg of 0.5% hyperbaric ropivacaine (group HR, n=30) and the third group received 15 mg of 0.5% hyperbaric levobupivacaine (group HL, n=30). They concluded that in 15 mg doses, hyperbaric levobupivacaine showed similar potency and block characteristics to hyperbaric bupivacaine. The duration of motor block was the longest in bupivacaine but not significantly different than levobupivacaine group. The duration of motor and sensory block was the shortest with hyperbaric ropivacaine. Levobupivacaine and ropivacaine had fewer side effects. Gozaydin O et al.[13] conducted study in in forty ASAI-II patients undergoing unilateral hernia operation under spinal anesthesia compared hyperbaric bupivacaine with the same amount of hyperbaric levobupivacaine (3 ml 0.5% solution). In conclusion, they stated that features of levobupivacaine for anesthetic effect, hemodynamic parameters, postoperative analgesic requirement time, and the first 24-hour side effects and complications were similar to hyperbaric bupivacaine. Therefore, it was suggested that hyperbaric levobupivacaine may be an alternative to hyperbaric bupivacaine for spinal anesthesia.

Conclusion

Our study reveals that 15 mg of isobaric Levobupivacaine (3ml of 0.5%) when administered intrathecally provides adequate anesthesia for lower abdominal surgeries. Onset of sensory block is slow compared to that of Bupivacaine, with same level of maximum sensory block. The duration of analgesia at L4 (L4 regression) was significantly same with Levobupivacaine. But there is delayed onset of motor block and shorter duration of motor block with levobupivacaine compared to Bupivacaine. Cardiovascular stability is better than Bupivacaine. Hence Levobupivacaine can be used successfully for lower abdominal surgeries where early recovery is well appreciated by the patients.

References

1. Heavner JE. Cardiac toxicity of local anesthetics in the intact isolated heart model: a review. Reg Anesth Pain Med 2002; 27(6):545-555.
2. Strichartz GR, Berd CB. Local Anesthetics. In: Ronald D. Miller(ed) Millers' Anesthesia. 7th ed . Philadelphia: Churchill Livingstone; Elsevier Inc, 2010; 913-940.
3. Glaser C, Marhofer P, Gabriela Zimpfer, Heinz M T, Sitzwohl C, Kapral S, Ingrid Schindler. Levobupivacaine versus Racemic Bupivacaine for spinal anaesthesia- Anesth Analg 2002; 94: 194-8.

4. Luck J.F, Fettes P.D.W, Wildsmith J.A.W. Spinal anaesthesia for elective surgery: A comparison of hyperbaric solutions of racemic bupivacaine, levobupivacaine, and Ropivacaine. Br J Anaesth 2008; 101(5): 705-10.
5. Alley AE, Kopacz DJ, McDonald SB, Liu SS.Hyperbaric spinal levobupivacaine: a comparison to racemic bupivacaine in volunteers. Anesth Analg 2002; 94: 188-93.
6. Coppejans H C, Vercauteren M P. Spinal levobupivacaine for caesarean section causes less hypotension and motor block than racemic bupivacaine. Int J obstet Anesth 2004;13:S16.
7. Casati A, 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;99:1387-92.
8. Vanna O, Chumsang L, Thongmee S. Levobupivacaine and bupivacaine in spinal anesthesia for transurethral endoscopic surgery. J Med Assoc Thai 2006;89:1133-9.
9. Lee YY, Muchhal K, Chan CK. Levobupivacaine versus racemic bupivacaine in spinal anaesthesia for urological surgery. Anaesth Intensive Care 2003;31:637-41.
10. G. Frawley, K.R. Smith, P. Ingelmo,: Relative potencies of bupivacaine, levobupivacaine, and ropivacaine for neonatal spinal anaesthesia, British Journal of Anaesthesia,Volume 103, Issue 5,2009,Pages 731-738,
11. Hakan Erbay R, Ermumcu O, Hanci V, Atalay H. A comparison of spinal anesthesia with low-dose hyperbaric levobupivacaine and hyperbaric bupivacaine for transurethral surgery: A randomized controlled trial. Minerva Anestesiol 2010;76:992-1001.
12. Kazak Bengisun, Züleyha & Yilmaz, Ali & Özgencil, Enver & Tinazdoner, E & Okten, Furkan & Demiralp, S. (2006). 160Comparison of plain and hyperbaric solutions of ropivacaine and bupivacaine for spinal anesthesia for major orthopedic surgery. Regional Anesthesia and Pain Medicine. 31. 41-41.
13. Gozaydin, Guven Gulen, Guneri Atalan , Mehmet Kaydul: Comparison of Hyperbaric Levobupivacaine with Hyperbaric Bupivacaine in Unilateral Inguinal Hernia Operations Performed Under Spinal Anesthesia Orhan Arch Clin Exp Surg 2014;3:1-9