ORIGINAL ARTICLE

Comparative evaluation of clinical efficacy of intrathecal isobaric levobupivacaine and isobaric bupivacaine in patients undergoing infra-umbilical surgery

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ABSTRACT

Background and Aims: Levobupivacaine is a relatively new long-acting local anesthetic, which is the isolated S-enantiomer of racemic bupivacaine with less cardiotoxicity and neurotoxicity than bupivacaine. Although it has been introduced for routine epidural anesthesia, yet there is inadequate data for its use in infra-umbilical surgery under spinal anesthesia. We therefore performed this prospective randomized double-blinded study to evaluate the anesthetic potencies and hemodynamics of intrathecal levobupivacaine compared with racemic bupivacaine.

Methodology: A prospective randomized comparative double blind study included 100 patients, American Society of Anesthesiologists (ASA) I-II, scheduled for elective infra-umbilical surgeries under spinal anesthesia was done. The patients were divided into two groups which received either 3.5 ml levobupivacaine 0.5% isobaric or 3.5 ml bupivacaine 0.5% isobaric for spinal anesthesia. The measurement included vital signs, motor and sensory blockade and side effects.

Results: There was no significant difference between the two groups in the quality of motor and sensory block (p-value > 0.05). Maximum number of patients (60%) in levobupivacaine group had sensory onset time between 1-5 minutes whereas in bupivacaine group, 56% of patients had sensory onset time of 6-10 min, which was statistically significant (p=.0001). Nausea, vomiting and shivering was more in Group B patients.

Conclusion: The present study indicated that levobupivacaine is a valid alternative to racemic bupivacaine for spinal anesthesia. Both the drugs have similar clinical profile, requirement of rescue analgesic and side effect such as hemodynamic changes, nausea and vomiting.

Key words: Bupivacaine; Levobupivacaine; Local Anesthetics; Spinal Anaesthesia

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INTRODUCTION

Spinal anesthesia is one of the most commonly used technique for infra-umbilical surgeries because of its unquestionable reliability, effective analgesia, cost effectiveness, muscle relaxation and prolonged postoperative analgesia.[1] An anesthetic agent should have low incidence of anesthetic complications, adequate postoperative analgesia and allow early patient discharge for day care surgeries in spinal anesthesia.[2,3] Levobupivacaine is a S(-)-isomer of the racemate bupivacaine

and relatively new amino amide. In recent years levobupivacaine has emerged as a safer alternative for bupivacaine because of reports of cardiovascular and central nervous toxicity due to bupivacaine. It was shown that potential for toxicity was higher with D-isomer of bupivacaine therefore it was thought that if it was possible to use only levo rotatory isomer of bupivacaine that is levobupivacaine, risk for cardiotoxicity and neurotoxicity could be less but with similar clinical effects.[4,5] In one Cochrane review both hyperbaric bupivacaine without adjunct and isobaric bupivacaine-without adjunct provides effective subarachnoid block for surgical procedure and large randomized trial is needed to confirm before a switch from isobaric bupivacaine to hyperbaric bupivacaine can be recommended.[6] In one study levobupivacaine and racemic bupivacaine had shown equally effective potencies for spinal anesthesia, both with regard to the onset time and the duration of sensory and motor blockade. Indeed, levobupivacaine generally showed a more sustained sensory and motor blockade.[7] Intrathecal administration resulted in comparable similar hemodynamic changes in both levobupivacaine and racemic bupivacaine.[8] Because of above facts, for spinal anesthesia levobupivacaine seems to be an interesting alternative to bupivacaine. Levobupivacaine can be used for all indications in which the anesthetist needs a long acting local anaesthetic with an added advantage of reduced toxicity for the patient. Recently equipotency of levobupivacaine and racemic bupivacaine has been questioned, prompting anesthetist to increase the dose of levobupivacaine in an attempt to ensure adequate anesthesia and analgesia and offsetting, therefore, the advantages of less motor block with levobupivacaine.[9,10] Therefore the present study was conducted to evaluate and compare the efficacy of intrathecal levobupivacaine and bupivacaine in the patients undergoing infra-umbilical surgeries under spinal anesthesia.

METHODOLOGY

After an Institutional Ethical Committee approval, 100 patients aged 18-80 years, American Society of Anesthesiologists (ASA) physical status class I or II, were enrolled into this prospective randomized, comparative double-blind study during the period from April 2013 - December 2014. Patients unwilling for the procedure, those with coagulation or neurological disorders, anatomical deformities on back or local infection on site of spinal, patients on anticoagulant therapy, those with allergy to local anesthetics or with a history of chronic pain, neuropathy, as well as obese or pregnant women were excluded.

A written informed consent was taken from all the patients scheduled for infra-umbilical surgeries. Patients were randomized into two Groups L and B using sealed envelope technique after explaining the nature and purpose of the study and obtaining informed consent from the patient.

Group B (n=50) received isobaric 0.5% bupivacaine (Anawin™, Neon Laboratories Ltd. UK) while Group L (n=50) received isobaric 0.5 % levobupivacaine (Chirocaine™: levobupivacaine hydrochloride, Abbott Laboratories, UK). The patients allocated to two groups received either 3.5 ml levobupivacaine 0.5% isobaric or 3.5 ml bupivacaine 0.5% isobaric for spinal anesthesia. A detailed pre anesthetic examination was done. Necessary investigations were done and informed consent was taken. All patients were premeditated with Tab alprazolam 0.25 mg, tab ranitidine 150 mg at the night before surgery and at 6 AM on the day of surgery with sips of water. Before surgery, patients were given instructions to use a 10-point visual analogue scale (VAS). Baseline Visual Analogue scale was recorded for the patients.

In the operating room, routine multipara monitors were attached, IV line was secured with 18 gauge intracath, preloading was done using ringer lactate (10 ml/kg) over 15-20 min. Two anesthetists were involved in this double-blind study: one prepared the anaesthetic solution assigned according to a random-number table by means of a computer-generated randomization list and performed the spinal block while the other, unaware of the anaesthetic solution in use, evaluated the study variables. Study drug was prepared in similar syringes keeping the drug volume constant and spinal block was done. Under all aseptic precautions lumbar puncture was performed in left lateral position L 3-4 or L 4-5 interspace via midline approach in lateral decubitus position. In Group L, 3.5 ml of 0.5% isobaric levobupivacaine and in Group B 3.5 ml of isobaric 0.5% bupivacaine was given through 26G Whitacre spinal needle. Patients were immediately turned to supine position and oxygen was administered via a facemask at 6 L/min. Bradycardia (defined as HR <20% from baseline) was treated with injection atropine sulphate 0.6 mg IV. Hypotension (defined as fall in SBP >20% from baseline) was treated with additional Ringer's lactate solution and injection mephenteramine 5 mg IV titrated according to blood pressure.

Thereafter, an investigator, blinded to the identity of the solution administered, assessed the upper and lower limits of sensory block (analgesia to pinprick using the short bevel end of a 27G needle: caudad limit of sensory block assessment, S2). The onset time of sensory block was assessed referring to the interval between spinal puncture and the maximal pinprick score. Sensory block was tested using loss of sensation to pin-prick in the present study. Motor block was assessed and recorded as per Bromage Scale. The time to onset of motor block, the time to reach Bromage 3 and the time of complete disappearance were recorded. All parameters were noted by taking the time of giving the study drug intrathecally as time 0. Surgery was allowed to start when sensory block to T10 dermatome was achieved. The quality of surgical analgesia was assessed and graded as: *Excellent* - no supplementary drugs required; *Good* - analgesic required; *Fair* - more than one analgesic required; *Poor* - general anesthesia required.

VAS scoring was done every 10 min till 30 min and thereafter every 15 min. If VAS score was > 3 then patient was given analgesic inj tramadol 50 mg. The duration of effective analgesia (time taken from intrathecal injection to first dose of rescue analgesic) was recorded. At point of time at which patient demanded first dose of rescue analgesia was taken as total duration of analgesia. Number of doses of rescue analgesia required in the postoperative period was also noted.

Any side effects or complications like dry mouth, nausea, vomiting, hypotension, bradycardia, sedation, urinary retention, pruritus, headache, backache and neurological changes for 24 hr was monitored in patients. Patient satisfaction score was generated by general questioning of the patients regarding their experience of anesthesia during intra- and post-operative period at the end of the study. It was analyzed as excellent, satisfactory or unsatisfactory; while satisfaction score of surgeon was analyzed as, excellent, satisfactory or unsatisfactory.

Sample size was determined as being consistent with previous similar studies so as to maintain the overall alpha error at < 0.0 5 and statistical power of at least 80%. Data thus collected were entered into a computer-based spreadsheet for analysis using SPSS statistical software (version 20) (IBM Corp., NY, USA). The statistical tests applied included proportions, Student's t-test, Fischer's exact probability test and Chi-square tests for significance of associations.

RESULTS

In the present study, both the study groups were comparable with respect to their demographic characteristics, baseline hemodynamic parameters and duration of surgery. The two groups in the present study were comparable in terms of age distribution. Maximum number of patients in both groups had body weight between 51-60 kg. Maximum number of patients in both groups underwent orthopedic, gynecological and lower abdominal surgeries (Table 1).

Table 1: Patient characteristics and details of surgery. Data presented as N (%)

Parameter	Group L	Group B
Mean age of patient (Mean ± SD)	36.5 ± 12.9	40.1 ± 13.6
Males	32 (64)	30 (60)
Females	18 (36)	20 (40)
Average weight (kg) (Mean ± SD)	60.7 ± 8.3	57.5 ± 7.2
Height (cm)		
Type Of Surgery		
Gynecological	15 (30)	10 (20)
Appendicectomy	5 (10)	8 (16)
Hernia	15 (30)	8 (16)
Anal	10 (20)	12 (24)
Orthopedic	3 (6)	3 (6)
Hydrocele/scrotal/varicocele	2 (4)	6 (12)
Urethral	0 (0)	3 (6)

Cardiovascular changes were unremarkable, with no statistically significant differences between the groups in heart rate, systolic arterial pressure, or the incidence of hypotension. In Group L mean baseline HR was 72.4 ± 8.9. There was significant reduction in heart rate from 60-90 min ($p < 0.05$). In Group B mean baseline was 72.45 ± 5.6. There was significant reduction in HR from 15 min-105 min ($p < 0.05$). Heart rate of both groups were compared and there was no statistically significant difference in heart rate ($p > 0.05$).

Mean baseline SBP was 122.80 ± 8.4 in Group L as compared to 120.8 ± 6.7 in Group B. In Group L, there was significant reduction in systolic B.P from 30-105 min ($p < 0.05$).In Group B, there was significant reduction in SBP from 15-90 min ($p < 0.05$). In Group L, Mean baseline DBP was 79.5 ± 6.4. There was significant reduction from 30-90 min ($p < 0.05$). In Group B, mean baseline DBP

Table 2: Sensory and motor block characteristics in Group L and Group B

Different Parameters	Group L	Group B	P value
Onset of sensory block to T10 dermatome (min)	5.9 ± 3.4	7.9 ± 3.5	p=.001
Maximum Level Of Sensory Block	T5-T6 (56%)	T5-T6 (60%)	p=.37
Time to maximum sensory level (min)	24.4 ± 6.05	25.2 ± 4.6	p=.664
Duration of sensory regression to T10 level (min)	129.6 ± 34.6	131.8 ± 50.8	p=.87
Duration of sensory regression to S2 level (min)	257.2 ± 51.5	271.20 ± 41.48	p=.352
Grade of motor block (Bromage scale):	3 ± 1	3 ± 1	p=.067
Time for maximum motor block (min)	5.2 ± 3.8	5.3 ± 5.1	p=.97
Motor blockage regression (min)	176.4 ± 24.8	179.4 ± 26.9	P =.83
Time to mobilization (min)	285.6 ± 32.0	306.7 ± 34.5	P =.76
Duration of analgesia (min)	177.2 ± 28.9	181.2 ± 41.4	p=.725

Group B received isobaric 0.5% bupivacaine, while Group L received isobaric 0.5 % levobupivacaine

was 79.4 ± 5.4. There were significant reduction in DBP from 15-90 min ($p < 0.05$).

Mean baseline MAP in Group L was 93.9 ± 6.5 as compared to 93.2 ± 4.8 in Group B. There was significant reduction from 30-105 min ($p < 0.05$). In Group B, there was significant reduction in MAP from 10-105 min ($p < 0.05$). When intergroup was compared, it was statistically insignificant ($p > 0.05$).

Maximum number of patients (60%) in levobupivacaine group had sensory onset time between 1-5 min whereas in bupivacaine group, 56% of patients had sensory onset time of 6-10 min (p=0.001) (Table 2). Time taken to achieve maximum level of sensory block was between 21-30 min for 90% of the patients in the Group B as compared to 80% patients in Group L. Only 6% patients in Group B took between 11-20 min as compared to 20% patients in Group L.

Mean VAS score in the levobupivacaine and bupivacaine group remained zero for 60 min after the administration of the drug. At 120 min mean VAS was 1.1 ± 0.4 for the levobupivacaine group as compared to 1.4 ± 0.8 for the bupivacaine group while at 180 min it was 2.4 ± 1.1 for Group L and 2.1 ± 0.9 for Group B. P = 0.02 and 0.006 for VAS score at 135 and 180 min respectively which was statistically significant. In maximum number of patients in Group L and Group B, VAS was more ≥ 3 at 180 min and they required rescue analgesia at 180 min.

6% patients in Group L experienced nausea and vomiting in comparison to 10% patients in Group B (p = 0.43). 6% patients in Group B as compared to 0% patients of Group L had shivering (p = 0.92). 10% patients of Group B as compared to 6% patients in Group L were administered antiemetic (p = 0.92). 10% of patients from Group B and 6% of patients from Group L were administered vasopressor (mephentermine) when there was hypotension, results were statistically insignificant (p = 1.00).

DISCUSSION

Spinal anesthesia is widely used for infra-umbilical surgeries. General anesthesia is associated with difficult airway and pulmonary aspiration associated increased morbidity and mortality while in comparison local anesthetics require large doses for epidural anesthesia. In this study no statistically significant intergroup difference was found in heart rate, mean systolic BP, mean diastolic BP, MAP which is comparable with this study.[11,12]

In this study, we found that sensory onset was faster with levobupivacaine as compared to bupivacaine. As regards the onset time of sensory blockade, our results are comparable with that of few studies which have reported that both bupivacaine and levobupivacaine have comparable sensory onset time.[13] Another similar study with levobupivacaine and bupivacaine in spinal anesthesia showed equally effective potencies for both the onset time and duration of sensory blockade which was comparable with present study.[14]

In our study, maximum level of sensory block achieved was T5-T6 in 56% of patients in Group L as compared to 60% of patients in Group B. 16% patients in Group L had reached T3-T4 level as compared to 20% patients in Group B. These results were comparable (p =0.37) to the results shown by various studies were no statistical difference in maximum cephalad spread of sensory

block between levobupivacaine and bupivacaine was found.[7,15]

The time at which rescue analgesia was required in the two groups was comparable as in other studies.[16] In our study grade of motor block according to bromage scale was grade 3 in all the patients of both the groups (p= 0.067) which was statistically not significant similar to a study by Camorcia et al.[17] In this study, time taken for maximum motor blockade was in between 1-10 min in maximum number of patients (96%) in both the Group L and B respectively. Mean time taken for Group L was 5.2 ± 3.8 min and for Group B was 5.3 ± 5.0 min (p = 0.97) as seen in some other studies. [15]

In other studies intergroup difference between levobupivacaine and bupivacaine were insignificant with regard to onset time and duration of motor blockade which was comparable with our study.[7,12]

Thongrong C et al[13] in their study found that there was no significant difference between the two groups with regard to both onset and duration of motor block (p > 0.05) which was comparable with this study. In one study[18] levobupivacaine (103 ± 56 min) provided motor block of shorter duration in comparison to bupivacaine (149 ± 67) (p = 0.02). This is in contrast to our study. This could be due to use of hyperbaric bupivacaine in their study, whereas we used isobaric bupivacaine.

The quality of relaxation was excellent in all the patients of Group L. It was excellent in 96% patients in Group B (p=0.96) as in other studies.[19] Nausea, vomiting and shivering was statistically not significant in between the groups. While with regards to hemodynamics, e.g. intra-operative hypotension, the study recorded no statistical intergroup difference.

In the present study levobupivacaine had a rapid onset of action as compared to bupivacaine with almost similar clinical efficacy as regards to the onset, level and sensory and motor block duration. Also administration of the time of rescue analgesic, quality of analgesia and muscle relaxation was similar with both levobupivacaine and bupivacaine.

CONCLUSION

The results of the present study conclude that levobupivacaine is a valid alternative to racemic bupivacaine for spinal anesthesia. Both the drugs have similar clinical profile, requirement of rescue analgesic and side effect such as hemodynamic changes, nausea and vomiting.

Conflict of interest: None declared by the authors

Authors' contribution:

IY-Concept, design, statistical analysis, manuscript preparation

SG: Concept, literature search, manuscript preparation & editing

CKD: Concept, manuscript review

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