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Subarachnoid Hyperbaric Bupivacaine and Isobaric Levobupivacaine: A Prospective Randomized Double Blind Comparative Study

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Abstract

Aim: The aim of our study was to compare the efficacy, block parameters and safety profile of intrathecal hyperbaric bupivacaine and isobaric levobupivacaine for urological surgery. *Methods*: Urological patients who were scheduled for elective surgery under spinal anesthesia were enrolled in two groups. Group A received intrathecal 2.5 ml of (0.5%) hyperbaric bupivacaine, while Group B received intrathecal 2.5 ml of (0.5%) isobaric levobupivacaine. Sensory & motor block parameters, hemodynamic parameters and adverse effects in patients of both the groups were recorded. *Results*: The onset of sensory block, motor block and duration of motor block was comparable in both groups. Maximum height of sensory block was significantly higher in hyperbaric bupivacaine group and duration of sensory block was significantly higher in group B. Hemodynamic stability was better with levobupivacaine compared to hyperbaric bupivacaine. Hypotension and bradycardia were more common with hyperbaric bupivacaine group. In addition, nausea was noticed more frequently with hyperbaric bupivacaine. Other side-effects such as headache, backache, itching, vomiting, and shivering were almost similar in both the groups. *Conclusion*: We conclude that isobaric levobupivacaine is superior to hyperbaric bupivacaine in terms of longer sensory blockade and shorter motor blockade and also that intrathecal use of isobaric levobupivacaine is hemodynamically more favorable than that of hyperbaric bupivacaine.

Keywords: Levobupivacaine; Bupivacaine; Isobaric; Hyperbaric; Urological Surgeries.

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Introduction

Spinal anaesthesia was pioneered in humans by a German surgeon Dr August Bier on August 15th 1898 using Quinke method of entering the intrathecal space [1]. Since then several refinements has been done in the field of drugs and technique which has evolved into the modern concept of spinal anaesthesia. It provides simple, effective and safe analgesia in the perioperative period. 0.5% hyperbaric bupivacaine (racemic mixture), an amide local anaesthetic is presently the most common drug used for spinal anaesthesia. Due to the adverse cardiac effects of racemic bupivacaine, several studies have been performed to find anesthetic compounds of lesser toxicity to take its place. S-bupivacaine (levobupivacaine) has been found to have lesser cardiovascular and central nervous system toxicity [2,3]. When given in epidural space levobupivacaine has been found to have decreased cardiotoxicity in cases of accidental intravascular injections [4]. When administered for spinal anaesthesia it has been shown to have less motor blockade in compare of bupivacaine [5].

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Although hyperbaric local anesthetic solutions have a remarkable record of safety, their use is not totally without risk [6-8]. To prevent unilateral or saddle blocks, patients have to move rapidly from the lateral or sitting position to supine position and after mobilization of the patients, extension or early return of the block may be seen. Hyperbaric solutions may cause sudden cardiac arrest after spinal anesthesia because of the extension of the sympathetic block [9,10]. The use of truly isobaric solutions may have less sensitivity to position issues. Hyperbaric solutions may cause hypotension or bradycardia after mobilization; isobaric solutions are favored owing to their less sensitivity to position issues properties [11].

In this study we compared the clinical effects of 2 drugs hyperbaric bupivacaine and isobaric levobupivacaine in spinal anaesthesia for elective urological surgeries.

Materials and Methods

This study was conducted at Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India after taking approval from the Institutional ethics Committee and getting it registered with clinical trial registry of India viz. registration number CTRI/2017/10/010087. The duration of study was 8 months and was done from October 2017 to June 2018. With written informed consent100 adult patients of ASA grade I & II, Aged between 30-60 years undergoing urological surgeries under spinal anaesthesia were included in this study.

After routine preoperative evaluation and investigation, Persons with pre-existing neurological or spinal disease, cardiovascular, respiratory, renal, hepatic or any other systemic disease, Bleeding diathesis, Infection at the site of block, abnormalities of the spine, allergic to local anaesthetics, aspirin ingestion in the preceding week were excluded from the study.

Study design was taken as Prospective double blind Randomized clinical study. 100 patients were divided into two groups by computer generated random number method. Each group consisted of 50 patients. GROUP A patients were given 2.5 ml 0.5% hyperbaric bupivacaine whereas GROUP B patients were given 2.5 ml 0.5% isobaric levobupivacaine .

On the day of surgery, patients were shifted to the operation theatre with an 18 G IV cannula secured and they were preloaded with Ringer Lactate 10 ml/kg approximately 20 minutes prior to the administration of spinal anaesthesia. Non-invasive blood pressure monitor, pulse oximeter and ECG leads were connected to all patients and baseline values were recorded. Supplementary oxygen was provided at the rate of 5 liters/min via a face mask. Under strict aseptic precautions 2.5ml of the study drug was loaded by an anesthesiologist not involved in the study. Therefore, the patient and the anesthesiologist performing the spinal block and recording the intraoperative and postoperative data were blinded. The study drug was injected into L3-L4 sub arachnoid space using 26G whitacre spinal needles after confirming free flow of cerebrospinal fluid and the time of injection was recorded as 0 minutes. Following this the patients were made to lie supine immediately. Surgery was commenced after loss of sensation to pinprick at T6 level.

Following Parameters were noted

1. *Onset of sensory block* –Time taken from injection of study drug (0 minutes) to loss of sensation to pin-prick at T6 level. It was tested using a blunted 24G hypodermic needle bilaterally in the mid-clavicular line every 2 minutes.
2. *Maximum sensory block attained* – Time taken from injection of study drug (0 minutes) till the patient attained loss of sensation at the highest dermatome in 10 minutes. It was tested every 2 minutes using a blunted 24G hypodermic needle bilaterally in mid-clavicular line for the first 10 minutes. Time taken to reach the highest level of block was recorded.
3. *Duration of sensory block* – Time taken from maximum block height attained till regression of block to T10 dermatome. It was tested at the end of surgery using a 24G hypodermic needle bilaterally in mid-clavicular line.
4. *Onset of motor block* –Time taken from injection of study drug (0 minutes) till the patient attained Bromage 2. It was tested using modified Bromage scale every 2 minutes (0 = no paralysis, able to flex hips/knees/ankles; 1 = able to move knees, unable to raise extended legs; 2 = able to flex ankles, unable to flex knees; 3 = unable to move any part of the lower limb).
5. *Duration of motor block* – Time taken from maximum Bromage score attained to Bromage 0. It was tested at the end of surgery using modified Bromage scale.
6. *Hemodynamic changes* - Heart rate, systolic and mean arterial pressure and oxygen saturation were recorded every 5 minutes till the completion of

surgery and every 10 minutes postoperatively till the regression of sensory and motor block.

Management of Side Effects

Hypotension – drop in > 20% mean arterial pressure from baseline was treated with intermittent doses of IV mephenteramine. Total vasopressor dose required was recorded.

Bradycardia – drop in heart rate > 20% from baseline or values < 50 bpm was treated with IV atropine 0.01mg/kg stat. Total atropine dose administered was recorded.

Nausea/vomiting – was treated with IV ondansetron 4mg stat.

Patients were monitored for 6 hours in the postoperative ward for any adverse effects.

Blinding

Two Anaesthesiologists were involved in each case enrolled in this study. One Anaesthesiologist was engaged in preparation of drug and to allot a random number to the patient in that study. Second Anaesthesiologist was blinded to the study drug being given and was recording all the data for that case.

Statistical Analysis

Data were entered into Microsoft Excel spread sheet. Sample size was calculated using lambda willis formula based on data of previous studies. With power of study 80% and alpha error 5%, the sample size came to 42 for each group. Considering drop outs, 50 patients were recruited in each group. SPSS for Windows 21 (SPSS, Chicago, IL, USA) was used for statistical analysis. Continuous variables were analyzed with the unpaired t test and categorical variables were analyzed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $p < 0.05$.

Results

There has been no statistical difference between groups in terms of their demographic characteristics and the duration of the operation (Table 1 & Figure 1). One case in Group A and two case of Group B had failed spinal block. They were given general anesthesia and were excluded from the study. So 49 patients in Group A and 48 patients in Group B were analyzed for results. Both groups had achieved sufficient level of anesthesia and intraoperative analgesia and did not require additional analgesics.

The onset of sensory block, motor block and duration of motor block was comparable in both groups. Maximum height of sensory block was significantly higher in Group A while duration of sensory block was significantly higher in group B (Table 2 & Figure 2).

Table 1: Demographic profile

Variable	Group A	Group B	p-value	remarks
Age (yrs.)	48 ± 9.87	48.7 ± 9.18	0.871	Non-significant
Weight (kgs)	63.5 ± 7.82	62.7 ± 6.7	0.809	Non-significant
Sex (M/F)	33/16	34/14	0.628	Non-significant
Duration of surgery (mins)	50.9 ± 6.57	50.4 ± 6.73	0.868	Non-significant

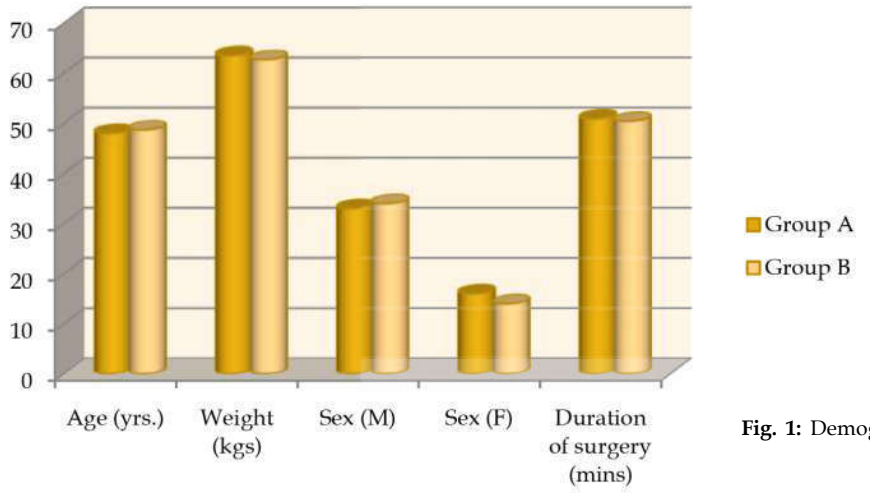

Fig. 1: Demographic profile

Hemodynamic stability was better with levobupivacaine compared to hyperbaric bupivacaine. Hypotension and bradycardia were more common with hyperbaric bupivacaine group. In addition, nausea was noticed more frequently with hyperbaric bupivacaine. Other side-effects such as headache, backache, itching, vomiting, and shivering were almost similar in both the groups. (Table 3 & Figure 3).

Table 2: Anesthesia characteristics

Variables	Group A	Group B	p-value	Remarks
Onset of sensory block (mins)	2.2 ± 0.42	2.6 ± 0.84	0.196	Non-significant
Maxim ht of sensory block (T level)	6.9 ± 0.74	6.3 ± 0.48	0.045	significant
Duration of sensory block (mins)	142.6 ± 8.33	156.6 ± 7.26	0.0008	Extremely-significant
Onset of motor block (mins)	3.25 ± 0.43	3.65 ± 0.54	0.083	Non-significant
Duration of motor block (mins)	114.1 ± 7.83	109.1 ± 5.67	0.119	Non-significant

Table 3: Side effects profile

Variables	Group A	%age	Group B	%age
Hypotension	28	56%	13	26%
Bradycardia	13	26%	3	6%
Headache	2	4%	1	2%
Nausea	8	16%	6	12%
Vomiting	4	8%	2	4%
Sedation	0	0	0	0
Itching	1	2%	1	2%
Backache	1	2%	0	0
Shivering	3	6%	2	4%

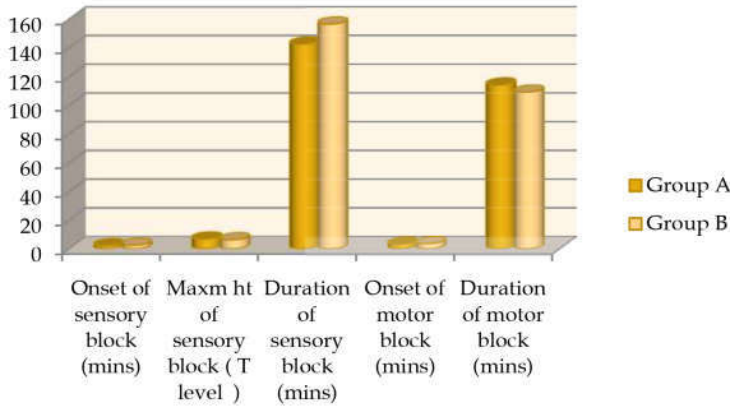

Fig. 2: Anesthesia characteristics

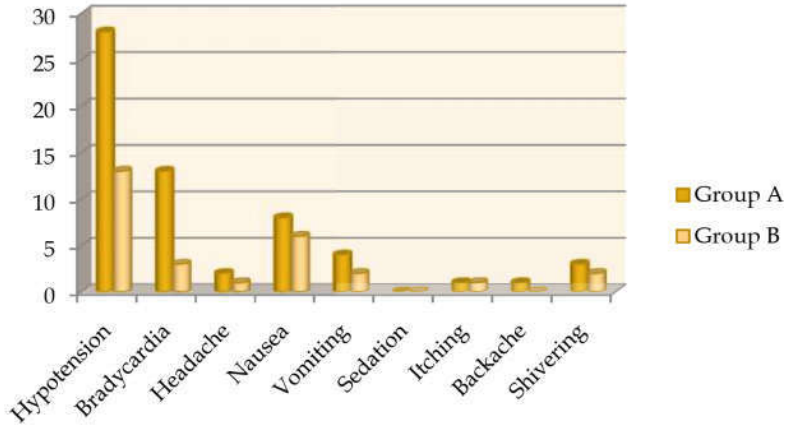

Fig. 3: Side effects profile

Discussion

In this study we compared the same doses of hyperbaric bupivacaine and isobaric levobupivacaine with regard to their hemodynamic effects, sensory block, and motor block. Both the speed of onset and offset of motor and sensory blockade were relatively quicker with hyperbaric bupivacaine. The extent of maximal block was significantly higher in hyperbaric bupivacaine group and duration of sensory blockade was significantly higher in isobaric levobupivacaine group. Baricity, defined as the density of intrathecal anesthetic solution relative to cerebrospinal fluid density, is a major determinant of the extent of subarachnoid blockade. Although they commonly lead to a more limited sensory blockade than plain solutions, hyperbaric solutions tend to gravitate to dependent areas and produce efficient analgesia during surgery.

Vercauteren et al. [12] performed a study on patients who received either 0.125% levobupivacaine or 0.125% racemic bupivacaine and found that levobupivacaine led to less motor impairment compared to racemic bupivacaine and 0.5% hyperbaric racemic bupivacaine in intrathecal labor analgesia. This is in accordance with our study.

A study by Vana et al. [13] demonstrated that 2.5 mL of 0.5% isobaric levobupivacaine and 0.5% hyperbaric racemic bupivacaine showed equally effective potencies for spinal anesthesia in transurethral resection (TUR) surgery with regard to the onset of time and duration of sensory blockade. This is in contrast to our study.

In the present study, hypotension and bradycardia was found to be more in bupivacaine group. Erdil et al. [14] noted, in spinal anesthesia, better hemodynamic stability associated with low-dose levobupivacaine plus fentanyl compared with that seen with low-dose bupivacaine plus fentanyl. Coppejans and Vercauteren [15] compared equipotent doses of bupivacaine, levobupivacaine, and ropivacaine combined with sufentanil in patients undergoing elective CS with combined spinal–epidural anesthesia. They found that hemodynamic values were comparable between the three groups (although a trend towards better SBPs and a lower prevalence of severe hypotension were noticed with levobupivacaine). These are in accordance with our study. Guler et al. [16] reported that levobupivacaine, compared with bupivacaine, causes less bradycardia, and hypotension which is also observed in our study. Goyal et al. [17] went further to conclude that levobupivacaine with fentanyl should be the preferred alternative to bupivacaine. The present study differs from the above studies as no opioid has been combined to local anesthetic for intrathecal administration. In contrast, in a study comparing 10 mg hyperbaric bupivacaine, 11 mg levobupivacaine and 11 mg bupivacaine, all with 10 μg fentanyl given intrathecally for cesarean section, Sundarathiti et al. [18] found that there was no difference in hemodynamic parameters in any of the groups. Glaser et al. [19] compared 3.5 ml of 0.5% isobaric levobupivacaine to 3.5 ml of 0.5% racemic isobaric bupivacaine in 80 patients undergoing elective hip replacement. None of the 79 patients required sup-plemental analgesics during surgery. Cuvas et al. [20] compared 1 ml of 0.5% plain bupivacaine to 0.5% levobupivacaine for a subarachnoid block in patients undergoing pilonidal sinus sur-gery performed in the prone position. All patients who received bupivacaine and 92% of the patients who recievd levobupivacaine were satisfied with the quality of anaesthesia.

Conclusion

In conclusion to our study we noticed that isobaric levobupivacaine is superior to hyperbaric bupivacaine in terms of longer sensory blockade and shorter motor blockade and also that intrathecal use of isobaric levobupivacaine is hemodynamically more favorable than that of hyperbaric bupivacaine.

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